EXHIBIT 18

US006146361A

United States Patent [19]

DiBiasi et al.

[11] Patent Number: 6,146,361

[45] Date of Patent: *Nov. 14, 2000

[54] **MEDICATION DELIVERY PEN HAVING A 31 GAUGE NEEDLE**

[75] Inventors: **Michael D. DiBiasi**, West Milford; **Elizabeth A. Harbin**, Wayne; **Robert E. West**, Morristown, all of N.J.

[73] Assignee: **Becton Dickinson and Company**, Franklin Lakes, N.J.

[*] Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

[21] Appl. No.: **08/721,368**

[22] Filed: **Sep. 26, 1996**

[51] **Int. Cl.**[7] **A61M 5/00**

[52] **U.S. Cl.** **604/232**; 604/272

[58] **Field of Search** 604/232, 233, 604/234, 272, 207, 208, 211, 187

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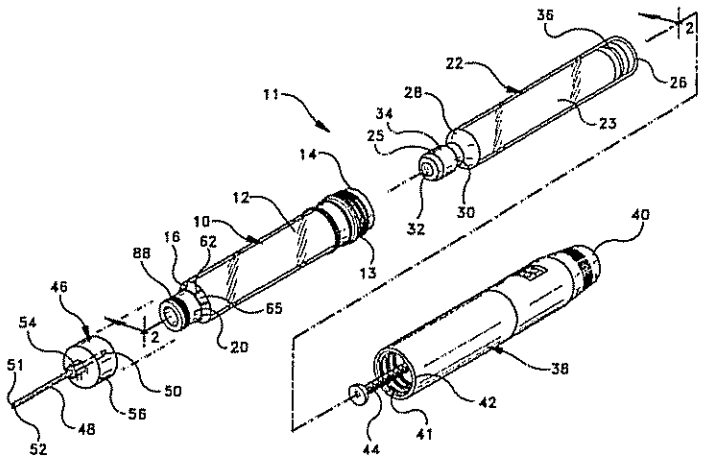
Primary Examiner—John D. Yasko
Attorney, Agent, or Firm—Alan W. Fiedler

[57] **ABSTRACT**

A needle assembly for a medication delivery pen having a 31 gauge needle cannula that reduces penetration force during an injection process resulting in less pain to the patient without causing any loss in performance or structural integrity.

9 Claims, 2 Drawing Sheets



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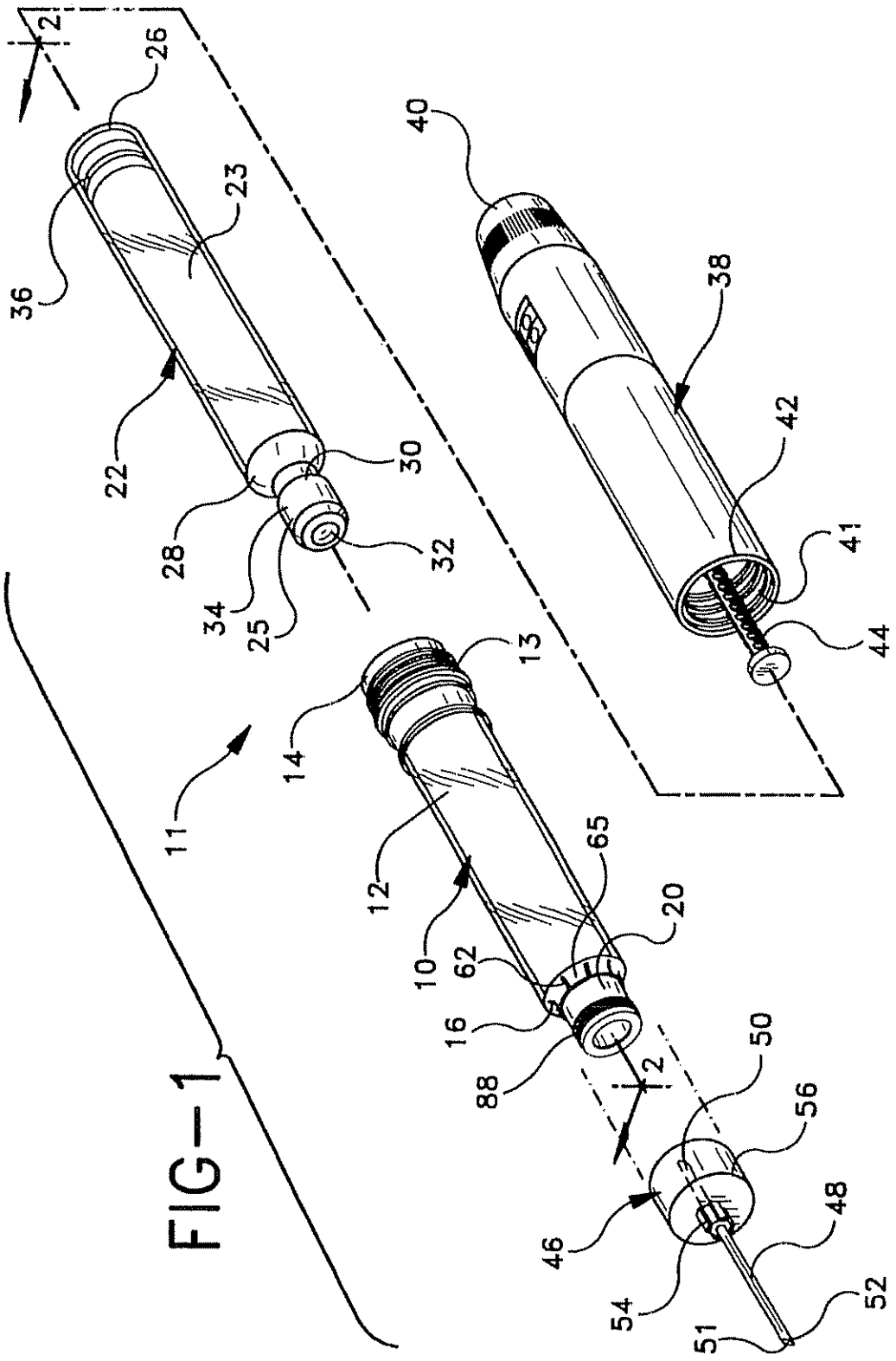
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FIG-1

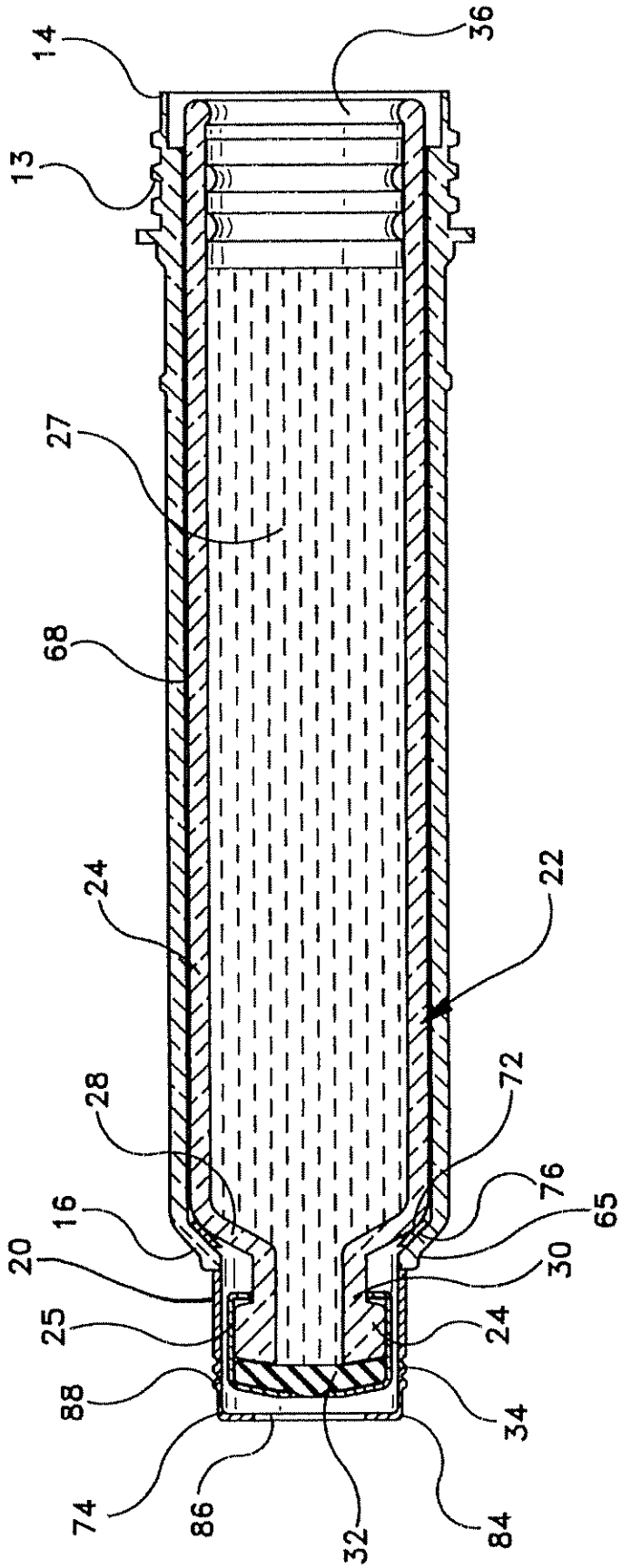

FIG-2

MEDICATION DELIVERY PEN HAVING A 31 GAUGE NEEDLE

BACKGROUND OF THE INVENTION

1. Field of the Invention

The subject invention relates to a medication delivery pen having a 31 gauge needle.

2. Background Description

Medication delivery pens are hypodermic syringes used for self-injection of precisely measured doses of medication. Pens are widely used, for example, by diabetics to dispense insulin.

A typical prior art medication delivery pen includes a cartridge which contains a volume of liquid medication sufficient for several doses. The cartridge includes an elongated generally tubular glass cartridge having a pierceable rubber septum which extends across the open distal end of the cartridge and is securely held in position by a metallic sleeve that is crimped to the distal end of the cartridge. The cartridge also includes a rubber stopper in sliding fluid-tight engagement with interior walls of the cartridge.

Such a medication delivery pen also includes a unitarily molded cartridge retainer having a small diameter tubular neck dimensioned for tightly engaging the neck of the cartridge and the metallic sleeve crimped thereon so as to support and position the entire cartridge. Exterior regions at the extreme distal end of the tubular neck are formed with an array of threads for threadedly receiving the mounting cap of a needle assembly. The medication delivery pen further includes a dosing apparatus that is engaged with the proximal end of the cartridge retainer having a plunger for engaging the rubber stopper of the cartridge. The dosing apparatus includes a dose setting structure used to select the longitudinal distance through which the plunger will move, and dispensing means for driving the plunger the selected distance.

The needle assembly for the medication delivery pen includes an elongate needle cannula having opposed proximal and distal points and a lumen extending therethrough. A plastic cork is adhered to an intermediate position along the needle cannula and in turn is rigidly connected to an end wall of a cylindrical cap. The cylindrical wall of the cap surrounds the proximal point on the needle cannula and includes an array of internal threads for engaging the external threads on the neck of the cartridge retainer.

The medication delivery pen may be used by urging the cap of the needle assembly over the neck of the cartridge retainer sufficiently for the proximal point of the needle cannula to pierce the rubber septum of the cartridge. The cap is then rotated to threadedly engage the neck of the cartridge retainer. The user then manipulates the dosing apparatus to select an appropriate dose. A protective shield over the distal end of the needle cannula is then removed, and the distal point of the needle cannula is injected. The user then actuates the dispensing means of the prior art dosing apparatus to urge the stopper of the cartridge distally and to deliver medication through the lumen of the needle cannula. The needle is then withdrawn, and the needle assembly is separated from the cartridge retainer and safely discarded. The rubber septum of the cartridge reseals itself, and may be pierced again for a subsequent administration of medication. This process may be carried out repeatedly until all of the medication in the cartridge has been used.

A problem with currently available needle assemblies for use on medication delivery pens is the size of the cannula.

Prior to the present invention, 27, 28, 29 and 30 gauge needle cannulas have been commonly used on medication delivery pens, with 30 gauge being the smallest diameter possible. Even though smaller gauges, i.e., 29 and 30 gauge, have helped to reduce pain to patients during injection, there is still a need to provide needle assemblies for medication delivery pens with smaller cannula diameters since small diameter needles are perceived by patients to cause less pain during the injection. However, no one skilled in the art has suggested and no one has provided patients with needle assemblies having a diameter less than 30 gauge.

SUMMARY OF THE INVENTION

The present invention overcomes the 30 gauge limit that has existed for pen needle assemblies by providing a 31 gauge needle assembly for use on medication delivery pens. The 31 gauge needle provides a patient with a needle assembly having a smaller cannula size without loss in performance or structural integrity. The 31 gauge needle assembly mounts on a needle mounting tip of a cartridge retainer assembly on a medication delivery pen and is used like prior art needle assemblies to pierce a patient's arm during an injection process.

However, since the 31 gauge needle cannula is smaller than prior art needle cannulas the penetration force is decreased which reduces the pain caused during an injection procedure. In addition, the smaller cannula size will be seen by the patient prior to the injection so that perceived pain or anticipated pain is also reduced. The reduction in actual and perceived/anticipated pain provided by using the 31 gauge needle on the medication delivery pen is a major benefit to patients that need numerous injections each day, i.e., diabetics requiring insulin injections.

These and other aspects, features and advantages of the present invention will become apparent from the following detailed description taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is an exploded perspective view of a medication delivery pen having a needle assembly in accordance with the subject invention; and

FIG. **2** is a cross-sectional view of a cartridge retainer assembly of the medication delivery pen.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

A needle assembly for use on a medication delivery pen **11**, in accordance with the subject invention, is identified generally by the numeral **46** in FIG. **1**. As shown in FIG. **1** medication delivery pen **11** includes a cartridge retainer assembly **10**, a dosing apparatus **38** and a cartridge assembly **22**. Needle assembly **46**, as described in more detail below, is designed to be attached to a needle mounting insert tip **20** on cartridge retainer assembly **10**.

Cartridge retainer assembly **10**, as shown in FIGS. **1** and **2**, includes an elongate generally tubular body **12** with opposed proximal and distal ends **14** and **16**, respectively. A generally tubular needle mounting insert tip **20** is snap-fit mounted in distal end **16** of body **12** and cartridge retainer assembly **10** is dimensioned and configured to receive a cartridge assembly **22** therein.

Cartridge assembly **22** includes an open proximal end **26** and a distal end **25** defined by an inwardly converging shoulder **28**. A small diameter neck **30** projects distally from

shoulder 28 on cartridge assembly 22, and is provided with a large diameter annular bead 24 extending circumferentially thereabout at the extreme distal end of neck 30. A pierceable and resealable rubber septum 32 extends completely across the open distal end defined by neck 30. Rubber septum 32 is held in place by a metallic sleeve 34 which is crimped around bead 24 at the distal end of neck 30. Medication such as insulin or heparin is pre-filled into cartridge assembly 22 and is retained therein by a rubber stopper 36. Stopper 36 is in sliding fluid-tight engagement with the tubular wall of cartridge assembly 22. Distally directed forces on stopper 36 urge the medication from pen 11 as explained further below.

Dosing apparatus 38 in medication delivery pen 11 is generally cylindrical and includes opposed proximal and distal ends 40 and 42, respectively. Threads 41 are disposed at distal end 42 of dosing apparatus 38 for releasable threaded engagement with proximal end 14 of body 12 of cartridge retainer assembly 10. A plunger rod 44 projects distally from dosing apparatus 38 and is dimensioned to engage stopper 36 of cartridge assembly 22. Dosing apparatus 38 also includes known mechanisms for setting a selected dose of medication to be delivered by pen 11. A dispensing mechanism (not shown) is operative to drive plunger rod 44 a selected distance in a distal direction for moving stopper 36 a distance that will inject the selected dose of medication from cartridge assembly 22. Although a particular prior art dosing apparatus 38 is depicted in FIG. 1, it is to be understood that other dosing apparatus can be used with the needle assembly of the subject invention.

Needle assembly 46, according to the present invention, includes a 31 gauge needle cannula 48 with opposed proximal and distal tips 50 and 52, respectively, and a lumen 51 extending entirely therethrough. The dimensions of 31 gauge needle cannula 48 are set forth below:

Parameter	Value
Outer Diameter	0.010"–0.0105"
Inner Diameter	0.0045"–0.006"
Wall Thickness	0.00225"–0.00275"
Usable length	0.315" (8 mm)
Cannula Material	Stainless Steel

Of course, 31 gauge needle cannulas of other lengths can also be used, i.e., 0.236" (6 mm) or 0.394" (10 mm), and still remain within the scope of the present invention. A cork 54 is securely affixed at an intermediate position along needle cannula 48, and a cap 56 is securely affixed to cork 54. Cap 56 of needle assembly 46 includes an array of internal threads (not shown) for removable mounting needle assembly 46 to needle mounting insert tip 20 on cartridge retainer assembly 10. It is to be understood, however, that other releasable engagement means between needle assembly 46 and cartridge retainer assembly can be provided. For example, external threads can be formed on needle assembly 46 and corresponding internal threads can be defined on cartridge retainer assembly 10 or a bayonet style mounting using lugs and slots can be used. In addition, needle assembly 46 could be "snap fit" on to cartridge retainer assembly 10.

As shown in FIG. 1, body 12 of cartridge retainer assembly 10 includes a plurality of inwardly projecting supports 65 separated from one another by notches 62, wherein supports 65 are used to hold insert tip 20 in distal end 16 of cartridge retainer assembly 10. FIG. 2 is a cross-sectional view of cartridge retainer assembly 10 that shows cartridge assembly 22 within a cartridge receiving chamber 68. FIGS. 1 and 2 also show an array of threads 13 on proximal end 14 of body 12 used to engage threads 41 on distal end 42 of dosing apparatus 38.

Needle mounting insert tip 20 of cartridge retainer assembly 10 includes opposed proximal and distal ends 72 and 74, respectively. As shown in FIG. 2, proximal end 72 of needle mounting insert tip 20 includes a rim 76 extending therefrom that is diametrically dimensioned to closely engage metallic sleeve 34 crimped to cartridge assembly 22 for holding rubber septum 32 in place. Distal end 74 of needle mounting insert tip 20 includes a generally annular end wall 84 having an aperture 86 extending therethrough for access by proximal point 50 of needle cannula 48. An array of outwardly disposed threads 88 is defined intermediate proximal and distal ends 72 and 74, respectively. Threads 88 are disposed and dimensioned for engaging threads on needle assembly 46.

Assembly of medication delivery pen 11 is performed by inserting cartridge assembly 22 into cartridge retainer assembly 10. More particularly, neck 30 and crimped metallic sleeve 34 of cartridge assembly 22 are inserted in a proximal to distal direction into open proximal end 14 of body 12 of cartridge retainer assembly 10. Crimped metallic sleeve 34 eventually will pass entirely through body 12, and further advancement of cartridge assembly 22 into cartridge retainer assembly 10 will require entry of crimped metallic sleeve 34 into rim 76 extending from proximal end 72 of needle mounting insert tip 20. Considerable dimensional variation and eccentricities between the neck and body of prior art cartridges are known to exist. If such eccentricities do exist, crimped metallic sleeve 34 will rest on rim 76 of insert tip 20 to center sleeve 34 relative to body 12 into a position that conforms with any dimensional inconsistencies or eccentricities in cartridge assembly 22.

Further distally directed movement of cartridge assembly 22 into cartridge retainer assembly 10 will cause shoulder 28 of cartridge assembly 22 to seat against rim 76 of insert tip 20. Rim 76 therefore defines the fully seated position of cartridge assembly 22 in cartridge retainer assembly 10 and functions to securely engage cartridge assembly 22. In this fully seated position, as shown most clearly in FIG. 2, septum 32 of cartridge assembly 22 is spaced proximally from distal wall 84 of needle mounting insert tip 20. Dosing apparatus 38 is then assembled to proximal end 14 of the body of cartridge retainer assembly 10 such that plunger rod 44 of dosing apparatus 38 engages stopper 26 of cartridge assembly 22.

Medication delivery pen 11 is used by mounting needle assembly 46 to needle mounting insert tip 20 of cartridge retainer assembly 10. This mounting is achieved by moving needle assembly 46 in a proximal direction over needle mounting insert tip 20 until the threads (not shown) of cap 56 engage external threads 88 on needle mounting insert tip 20. Threads 88 of needle mounting insert tip 20 are spaced from the extreme distal end of needle mounting insert tip 20, therefore, the initial axial advancement of cap 56 over needle mounting insert tip 20 will cause proximal point 50 of needle cannula 48 to pierce rubber septum 32 of cartridge assembly 22 prior to rotational threaded engagement of needle assembly 46 with needle mounting insert tip 20. Thus, the bevel which defines proximal point 50 will advance axially through septum 32 without a rotation that could tear rubber septum 32.

After threads of cap 56 engage threads 88 of needle mounting insert tip 20, further advancement of needle

assembly **46** requires relative rotation between cap **56** and needle mounting insert tip **20**. It will be appreciated that needle mounting insert tip **20** is too small to be readily griped by the user of medication delivery pen **11**, and is partly covered by cap **56**. However, the relative rotation can be achieved by rotating body **12** of cartridge retainer assembly **10**. Since needle mounting insert tip **20** is locked to distal end **16** on body **12** of cartridge retainer assembly **10**, rotation of body **12** is transmitted to needle mounting insert tip **20** and enables complete rotational engagement of needle assembly **46**.

Use of medication delivery pen **11** proceeds in a conventional manner with dosing apparatus **38**. Actuation of dosing apparatus **38** causes liquid medication in cartridge assembly **22** to be urged in a distal direction through lumen **51** of needle cannula **48**. This distally directed liquid pressure also will cause septum **32** to distend in a distal direction. However, as noted above and as shown in FIG. **2**, septum **32** is spaced proximally from cork **54** of needle assembly **46**, and will not be urged into contact with cork **54**. Thus, drooling or weeping of liquid medication can be substantially prevented. This is enabled because cartridge assembly **22** is supported and accurately positioned by engagement of cartridge shoulder **28** with rim **76** on insert tip **20**. Hence neck **30** and crimped metallic sleeve **34** need not be closely engaged by needle mounting insert tip **20**. After medication delivery pen **11** has been used, needle assembly **46** is separated from needle mounting insert tip **20** and discarded.

In the foregoing discussion, it is to be understood that the above-described embodiments of the present invention are simply illustrative of various features of a cartridge retainer assembly for a medication delivery pen. Other suitable variations, modifications and combinations of these features could be made to or used in these embodiments and still remain within the scope of the present invention.

What is claimed is:

1. A medication delivery pen for delivering medication to a patient during an injection procedure comprising:

a needle assembly having a 31 gauge needle cannula;

a cartridge assembly containing medication having a proximal and distal end, said proximal end including an array of threads and a stopper and said distal end including means for attaching said needle assembly so that medication can flow through said 31 gauge needle cannula during an injection procedure; and

a dosing apparatus having opposed proximal and distal ends with an array of threads at said distal end for threaded engagement with said threads at said proximal end of said cartridge assembly, said dosing apparatus further comprising a plunger rod projecting beyond said distal end of said dosing apparatus for selective engagement with said stopper in said cartridge assembly, and means for moving said plunger rod distally in said dosing apparatus selected amounts, whereby said plunger rod moves said stopper in said cartridge assembly to dispense medication from said cartridge assembly through said 31 gauge needle cannula.

2. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has an outer diameter less than 0.0105 inches.

3. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has an outer diameter no smaller than 0.010 inches and no larger than 0.0105 inches.

4. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has an inner diameter no smaller than 0.0045 inches and no larger than 0.006 inches.

5. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula is made of stainless steel.

6. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has a usable length of approximately 0.315 inches.

7. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has a usable length of approximately 0.236 inches.

8. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has a usable length of approximately 0.394 inches.

9. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has a wall thickness no smaller than 0.00225 inches and no larger than 0.00275 inches.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,146,361
DATED : November 14, 2000
INVENTOR(S) : Michael A. Dibiasi et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title page,
Item [56], **References Cited,** FOREIGN PATENT DOCUMENTS, insert
-- 279583B1 10/1993 European Pat. Off. --.
OTHER PUBLICATIONS, after "Novo Nordisk A/S":"Red Cassel" should read
-- Fred Cassel --.
Item [75], Inventors, "**Michael D. DiBiasi**" should read -- **Michael A. DiBiasi** --.

Column 3,
Line 50, "cap 56" should read -- cap or hub 56 --;
Line 52, "removable" should read -- removably --;
Line 56, "assembly" should read -- assembly 10 --.

Column 5,
Line 4, "griped" should read -- gripped --.

Column 6,
Line 42, insert
-- 10. An insulin injection system comprising a pen shaped syringe comprising a cartridge with insulin and an injection needle, wherein the needle is a 31 gauge needle and the cartridge contains an insulin type that may freely flow through a 31 gauge needle.

11. An insulin injection system according to Claim 10, wherein the pen shaped syringe is designed to receive cartridges containing insulin which may pass freely through a 31 gauge needle.

12. An insulin injection system according to Claim 10, wherein the needle has attaching means for cooperation with attaching means on the pen shaped syringe.

13. An insulin injection system according to Claim 12, wherein the needle attaching means is a needle hub having a thread cooperating with a corresponding thread on the pen shaped syringe.

14. An insulin injection system according to Claim 13, wherein the needle hub has a central protrusion covering part of the length of the needle.

15. An insulin injection system according to Claim 14, wherein the length of the injection part of the needle is 8mm.

16. An insulin injection system according to Claim 14, wherein the length of the injection part of the needle is 10mm.

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,146,361
DATED : November 14, 2000
INVENTOR(S) : Michael A. Dibiasi et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

17. A needle assembly comprising:

(a) a needle hub having a base and a needle fitting for removably mounting said needle assembly on a pen-type insulin syringe having a mounting and which accepts cartridges containing insulin that may flow freely through a 31 gauge needle; and

(b) a 31 gauge needle secured in said base and having first and second needle portions extending from said base in opposite directions.

18. A needle assembly according to Claim 17, wherein said needle fitting includes an annular sleeve extending from said base such that said sleeve surrounds said first needle portion concentrically and is spaced therefrom, and wherein said sleeve has a threaded interior by which it may be screwed onto an externally threaded hub-receiving part of a pen-type insulin syringe.

19. A needle assembly according to Claim 18, wherein said second needle portion has a predetermined length appropriate for injecting insulin into a human patient.

20. A needle assembly according to Claim 19, wherein said base further comprises a central protrusion which extends from said base for a predetermined distance along said second needle portion and embeds said second needle portion along the said distance, and wherein said second needle portion further comprises an exposed end which projects axially from said central protrusion and which has a length corresponding to the desired depth of needle insertion into a human patient. --

Signed and Sealed this

Seventeenth Day of December, 2002

JAMES E. ROGAN
Director of the United States Patent and Trademark Office

EXHIBIT 19

United States Patent [19]

Sams

[11] **Patent Number: 4,936,833**

[45] **Date of Patent: Jun. 26, 1990**

[54] **CARTRIDGE-HOLDER ASSEMBLY FOR MEDICATION DISPENSING UNIT**

[75] Inventor: **Bernard Sams**, London, England

[73] Assignee: **Hypoguard (UK) Limited**, Woodbridge, England

[21] Appl. No.: **237,147**

[22] Filed: **Aug. 26, 1988**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 205,198, Jun. 10, 1988, Pat. No. 4,865,591, which is a continuation-in-part of Ser. No. 81,241, Aug. 4, 1987, abandoned.

[51] **Int. Cl.**[5] **A61M 5/24**

[52] **U.S. Cl.** **604/232**; 604/208; 604/209; 604/220; 222/391

[58] **Field of Search** 604/68, 72, 208–210, 604/218, 220, 232, 234, 197; 222/325, 340, 391

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4,592,745	6/1986	Rex	604/211

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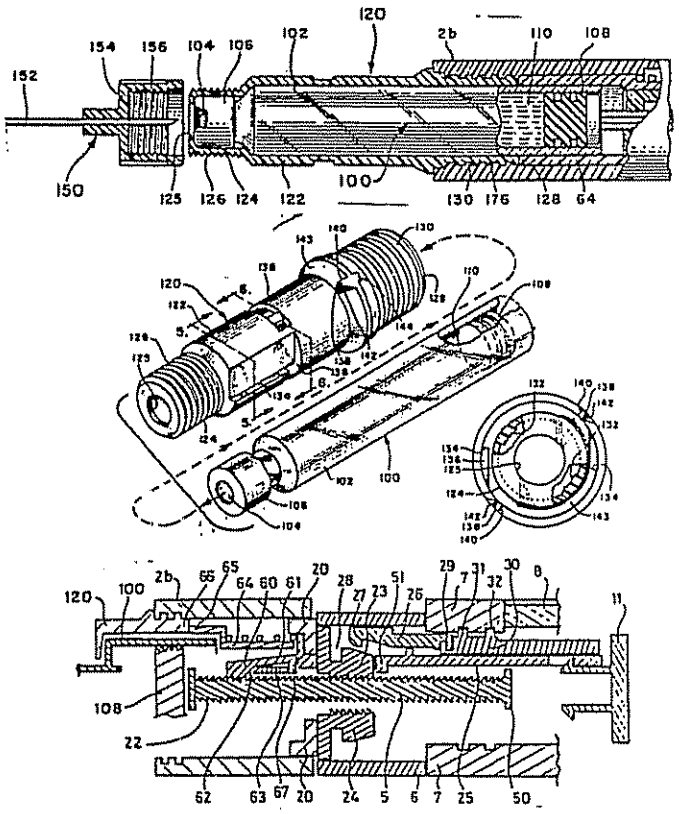
Primary Examiner—Martin P. Schwadron
Assistant Examiner—Allen J. Flanigan
Attorney, Agent, or Firm—Willian Brinks Olds Hofer Gilson & Lione

[57] **ABSTRACT**

A cartridge assembly for a syringe-type medication dispensing unit includes a cartridge having a cartridge body with first and second ends. A pierceable membrane is mounted at the first end and a piston is mounted at the second end, with a volume of medication contained in the cartridge body between the membrane and the piston. A cartridge holder receives the cartridge and defines first and second ends. The first holder end defines a central opening and an external thread for mounting a double-ended needle. The second holder end defines an external thread for securing the holder to a medication dispensing unit and an actuating shoulder. The holder frictionally engages the cartridge to form an assembly which can be handled as a single modular unit with the cartridge held securely in the holder by frictional engagement.

23 Claims, 6 Drawing Sheets



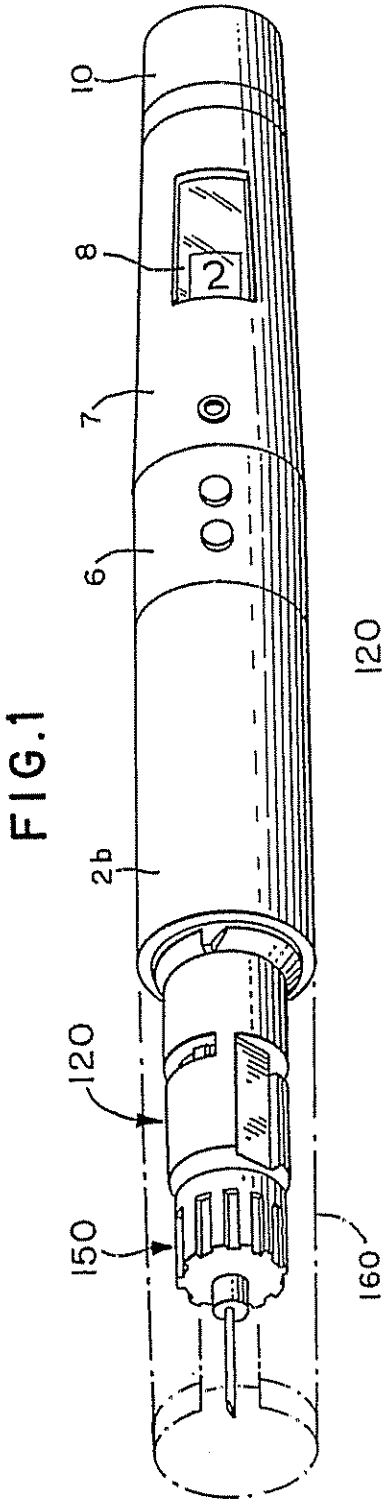

10
8
2
7
6
2b
120
150
160

FIG. 1

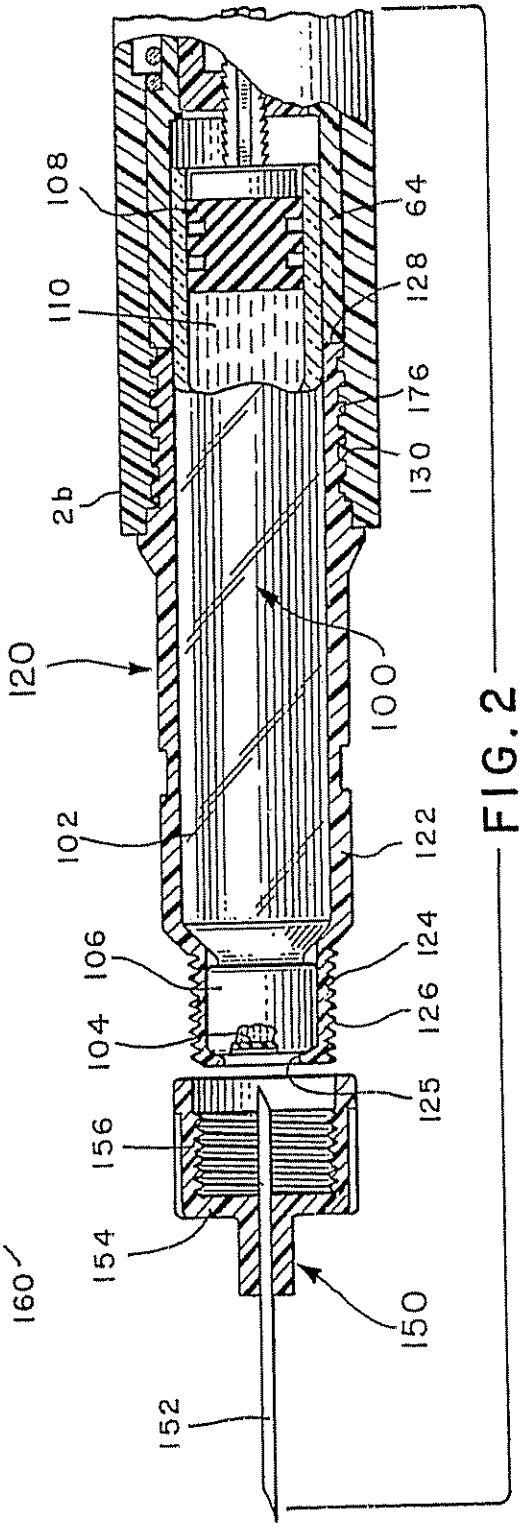

108
64
110
128
176
130
2b
120
100
102
122
106
124
104
126
125
156
154
150
152

FIG. 2

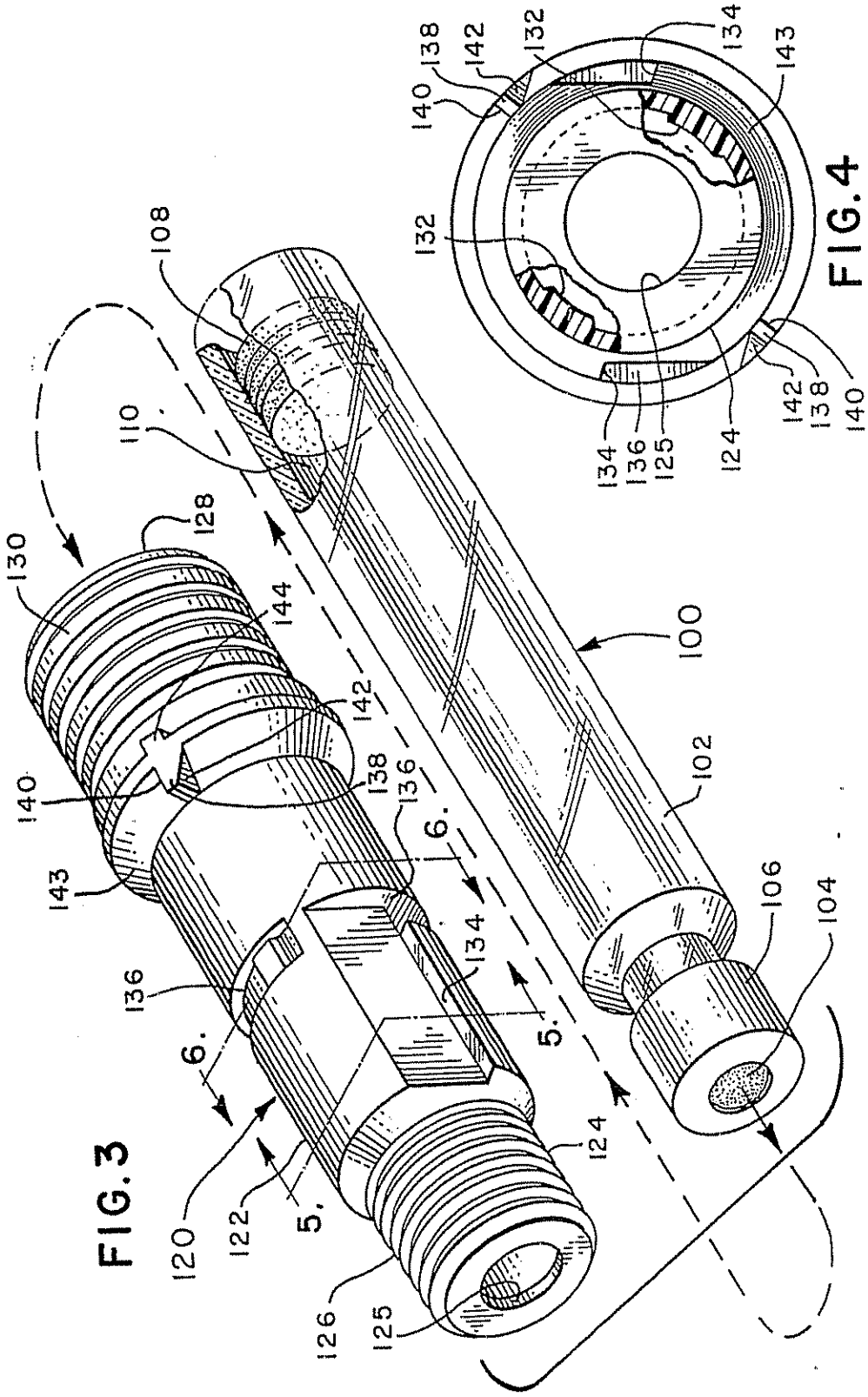

108
110
128
130
144
142
140
138
136
143
134
132
120
122
126
125
124
106
104
102
100
5.
6.

FIG. 3

138
142
132
134
143
140
132
142
138
140
134
136
125
124

FIG. 4

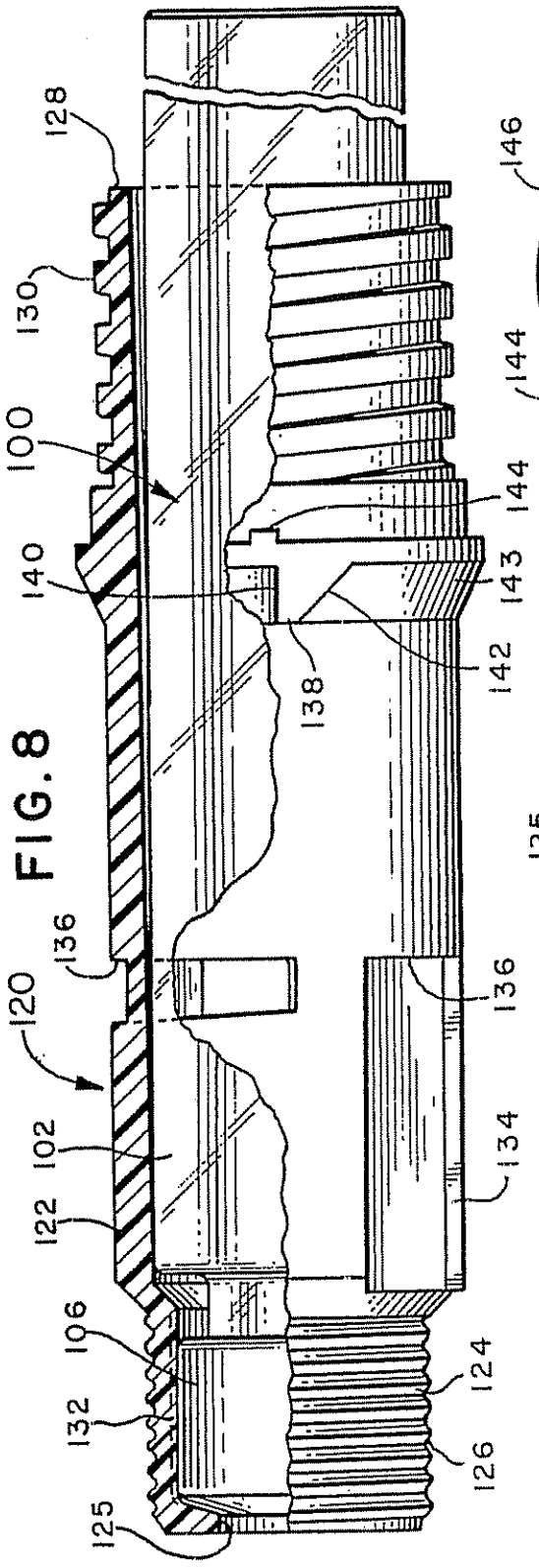


FIG. 8

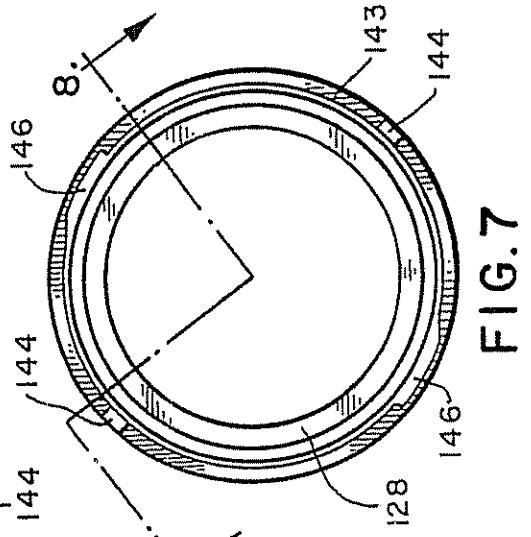


FIG. 7

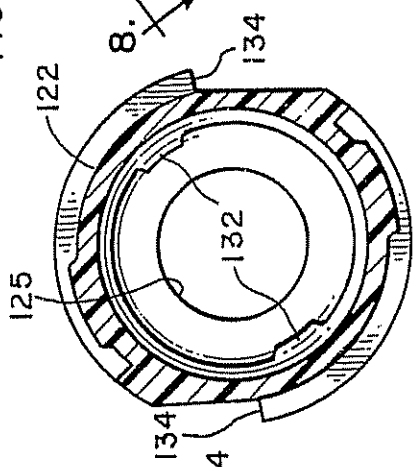


FIG. 6

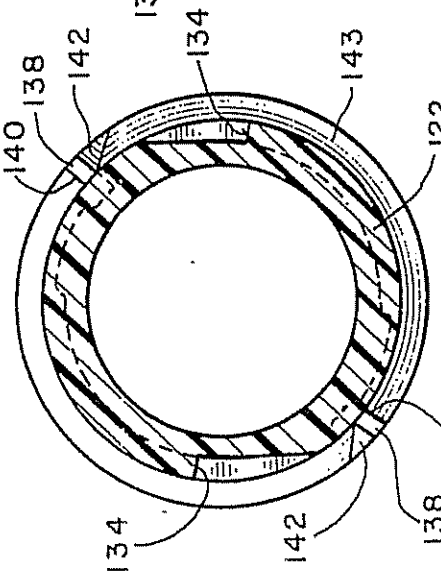


FIG. 5

FIG.9

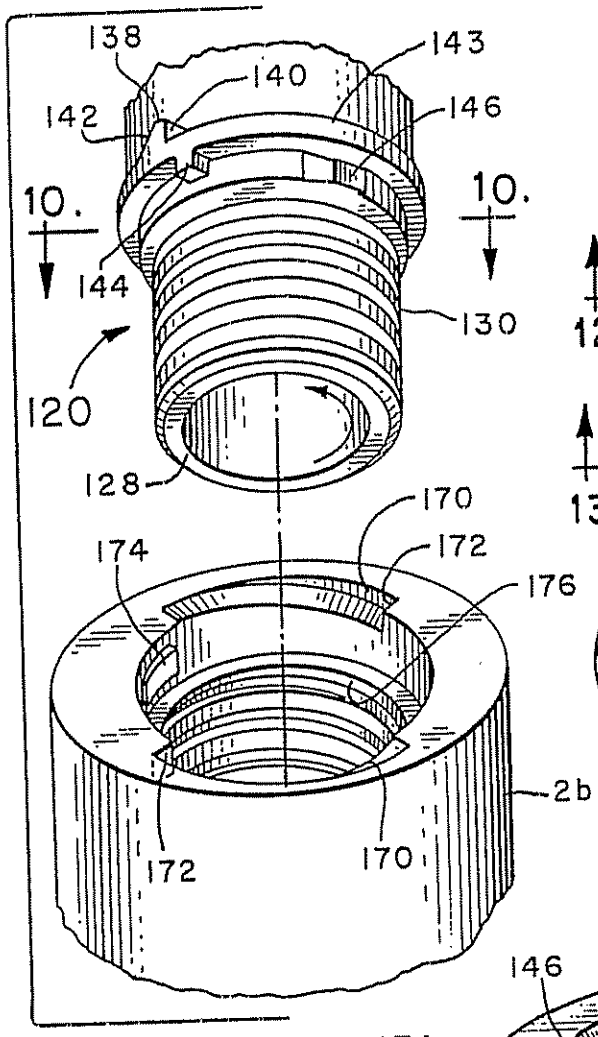
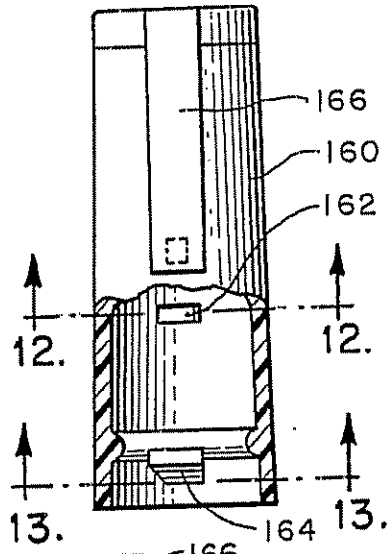


FIG.11



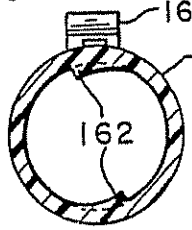


FIG.12

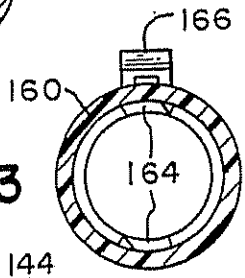


FIG.13

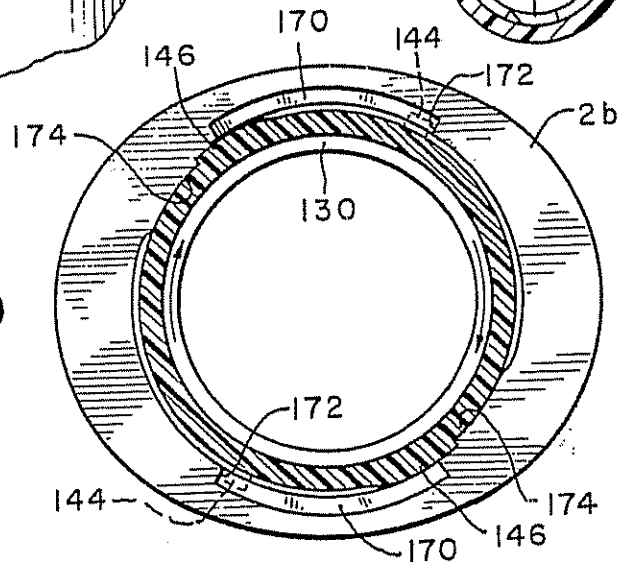


FIG.10

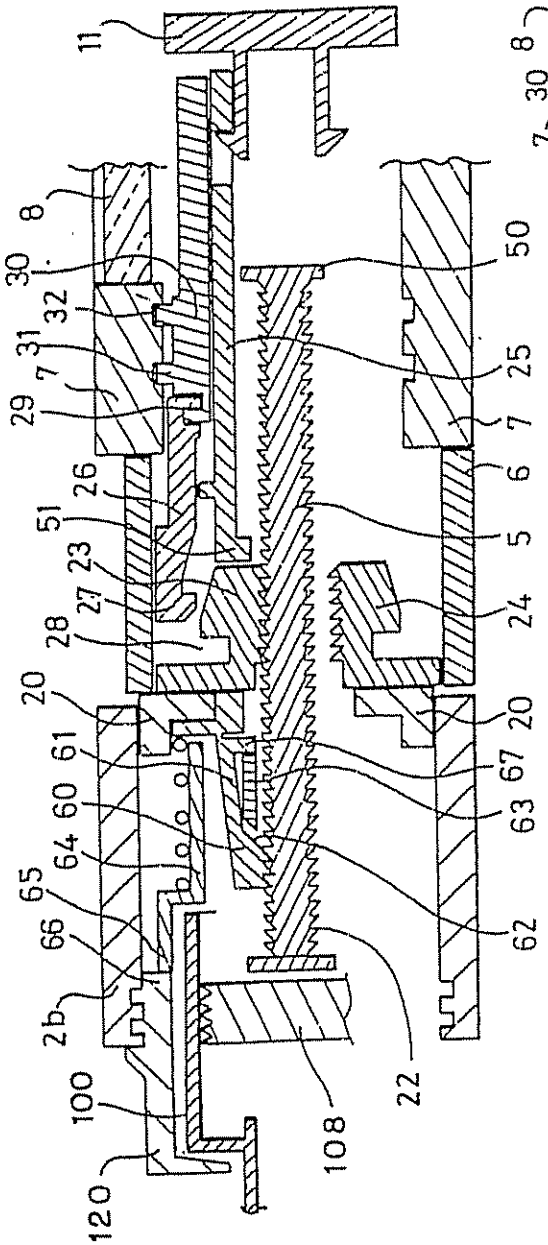

11
8
30
32
31
7
29
26
51
23
27
28
20
61
60
64
65
66
2b
100
120
108
22
50
25
7
6
5
24
20
67
63
62

FIG. 14

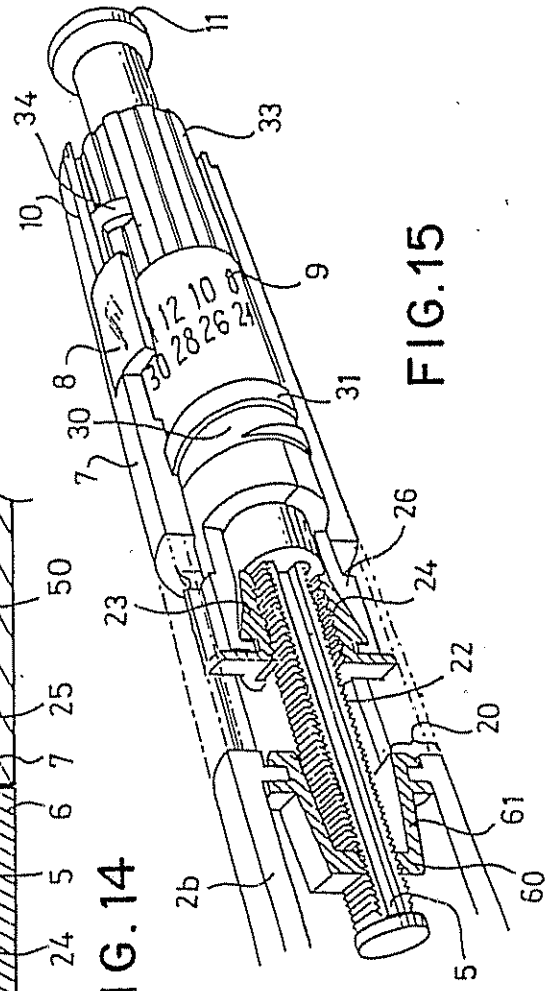

11
34
33
10
9
12
10
30
28
26
24
8
31
30
7
26
24
23
22
20
61
60
2b
5

FIG. 15

CARTRIDGE-HOLDER ASSEMBLY FOR MEDICATION DISPENSING UNIT

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of copending U.S. patent application Ser. No. 07/205,198, filed Jun. 10, 1988, now U.S. Pat. No. 4,865,591, which is in turn a continuation-in-part of U.S. patent application Ser. No. 07/081,241, filed Aug. 4, 1987, now abandoned. The entire text of these applications Ser. Nos. 07/205.198 and 07/081,241 is hereby incorporated by reference.

BACKGROUND OF THE INVENTION

The present invention relates to a cartridgeholder assembly for a measured dose medication dispensing device.

Patients suffering from diabetes often have to inject themselves with frequent doses of insulin and this can be done using a conventional syringe. However, such patients often also suffer from side effects of their illness and are not capable of accurately controlling the operation of such a syringe. It is therefore desirable that they should be provided with means for automatically administering an accurately controlled dosage. The dosage required by different patients can vary over quite wide ranges, from for example 2 units of insulin per dose to 30 or more units, and it is necessary to ensure that any device is capable of selecting a range of dosages simply and accurately.

Dispensing devices such as that shown in Rex U.S. Pat. No. 4,592,745 utilize a cartridge having a pierceable membrane at one end and a movable piston at the other, with a volume of a medication such as an insulin solution contained therebetween. The cartridge is mounted in a dispensing device which includes a plunger, a one-way mechanism that permits the plunger only to advance, and a mechanism for advancing the plunger to dispense medication.

The device disclosed in the Rex patent utilizes the rear rim of the cartridge to actuate the one-way mechanism: when the cartridge is removed the one-way mechanism releases, allowing the plunger to retract, but when the dispensing device is assembled with the cartridge in place the rear rim of the cartridge causes the one-way mechanism to engage the plunger. The cartridge is received loosely in a section of the device, and the one-way mechanism engaging apparatus resiliently holds the cartridge in position.

The dispensing device of the Rex patent has been proven effective and reliable in use. Nonetheless, it suffers from certain disadvantages related to the fact that the walls of the cartridge are formed of glass and in commercially practical cartridges it is difficult to control the overall length of the cartridge accurately. Resulting variations in the length of the cartridge cause the one-way mechanism to be engaged at a variable position as the cartridge enclosing section is screwed into place in the dispensing unit. If the cartridge is unusually long, the one-way mechanism will be engaged well before the cartridge enclosing section reaches its final position, and the plunger will then pressurize the contents of the cartridge as the section is screwed home. Such pressurization will produce a squirt of medication when the needle pierces the membrane. Some users may object to this unintended release of medication.

The variable length of the cartridge also imposes design constraints on the Rex dispensing device. As mentioned above, the cartridge fits loosely within the cartridge receiving section, and the cartridge is held in position by forces applied to the rear rim of the cartridge by the engaging apparatus for the one-way mechanism discussed above. This engaging apparatus must provide resilient support to the rim over the full range of cartridge lengths. Otherwise, the cartridge may be subjected to excessive axial forces, or it may alternately be left free to move axially in the dispensing device. The resilient mounting of the engaging apparatus in no way overcomes the problems discussed above related to unintended pressurization of the cartridge.

The present invention is directed to an improved cartridge-holder assembly that overcomes these prior art problems.

SUMMARY OF THE INVENTION

According to this invention, a cartridgeholder assembly is provided for a syringe-type medication dispensing unit. The cartridge comprises a cartridge body having first and second ends, a pierceable membrane mounted at the first end, and a piston mounted at the second end, with a volume of medication contained in the cartridge body between the membrane and the piston. The holder defines a first holder end which defines a central opening and means for mounting a double ended needle. The second holder end defines means for securing the holder to a medication dispensing unit and an actuating shoulder. The holder defines a central cavity shaped to receive and frictionally engage the cartridge to form an assembly that can be handled as a single, modular unit with the cartridge held frictionally in the holder.

This arrangement overcomes the prior art problems discussed above. The holder can easily be manufactured to high precision, and the actuating shoulder can therefore be accurately positioned to actuate the one-way mechanism just as the holder reaches its fully assembled position on the dispensing device. This substantially eliminates the problem of unintended pressurization of the cartridge before the needle is inserted into the membrane. Secondly, the releasable engagement between the cartridge and the holder allows the cartridge to be held in place without engagement of the rim. This relaxes design constraints on the engaging apparatus for the one-way mechanism.

As yet another advantage, the modular assembly of the holder and cartridge can be handled and assembled onto the dispensing device as a unit. This simplifies assembly by the patient.

The housing is preferably formed from a clear plastic material, and a user can therefore readily observe the movement of the piston within the cartridge and can assess the amount of medication in the cartridge. The housing also provides a measure of protection to the cartridge, both physical and against pathogenic organisms and other possible contamination.

The needle end of the cartridge can project through a terminal aperture in the housing or that end of the housing can be closed and can carry a needle or other outlet integrally therewith which projects axially inwardly into the housing to penetrate the membrane at the end of the cartridge.

The cartridge houses the piston which is to be moved by the plunger of the dispensing device. This piston can

be of conventional design and will usually form part of the cartridge as commercially available. The plunger acts on the piston and the piston can carry a socket or other recess to receive and locate the head of the plunger. In some cases, the plunger can be affixed to the piston and will form part of the cartridge as supplied, in which case the plunger will extend into the device when the cartridge is mounted on the device. However, it is preferred that the plunger form part of the device rather than of the cartridge and, for convenience the invention will hereinafter be described with respect to this configuration.

The invention itself, together with further objects and attendant advantages, will best be understood by reference to the following detailed description, taken in conjunction with the accompanying drawings

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective view of a syringe-type medication dispensing unit which includes a preferred embodiment of the cartridge-holder assembly of this invention.

FIG. 2 is a partial view of portions of the unit of FIG. 1 in partial section.

FIG. 3 is an exploded perspective view of the cartridge-holder assembly of FIG. 1.

FIG. 4 is a front view in partial cutaway of the holder of FIG. 3.

FIG. 5 is a cross sectional view taken along line 5—5 of FIG. 3.

FIG. 6 is a cross sectional view taken along line 6—6 of FIG. 3.

FIG. 7 is a rear view of the holder of FIG. 3.

FIG. 8 is a longitudinal sectional view taken along line 8—8 of FIG. 7 in partial elevation.

FIG. 9 is an exploded perspective view of portions of the dispensing device of FIG. 1.

FIG. 10 is a sectional view taken along line 10—10 of FIG. 9.

FIG. 11 is an elevational view in partial cutaway of the cap of FIG. 1.

FIG. 12 is a cross sectional view taken along line 12—12 of FIG. 11.

FIG. 13 is a cross sectional view taken along line 13—13 of FIG. 11.

FIG. 14 is a schematic cross sectional view of portions of the dispensing device of FIG. 1.

FIG. 15 is a perspective view in partial cutaway of portions of the dispensing device of FIG. 1.

DETAILED DESCRIPTION OF THE PRESENTLY PREFERRED EMBODIMENTS

FIGS. 1–10 show various views of the preferred embodiment of the cartridge-holder assembly of this invention, and FIGS. 11–15 provide further details relating to a preferred dispensing unit suitable for use with the cartridge-holder assembly of FIGS. 1–10.

Turning now to FIGS. 1–10, the preferred embodiment of the assembly of this invention comprises a cartridge 100 and a cartridge holder 120. FIG. 1 shows the holder 120 mounted to a dispensing device, and FIG. 2 shows the cartridge 100 mounted within the holder 120. As best shown in FIGS. 2 and 3, the cartridge 100 includes a generally cylindrical body 102 which is closed at one end by a pierceable membrane 104 and is sealed at the other end by a movable piston 108. A medication such as an insulin solution 110 is contained within the body 102 between the membrane 104 and the piston 108. In the conventional manner, a collar 106 of metal surrounds the membrane 104 and secures the membrane 104 to the body 102 in a fluid-tight manner.

The cartridge 100 can be quite similar to conventional glass cartridges. Of course, the dimensions of the cartridge should be chosen to match the dispensing device. Preferably, the body 102 is glass coated with silicone to reduce friction with the piston. The piston 108 is preferably about two-thirds the axial length of conventional pistons, also to reduce friction.

As best shown in FIGS. 2 and 8, the cartridge holder 120 comprises a tubular element 122 which defines a narrowed neck 124 which terminates in a central opening 125. External threads 126 are formed around the exterior of the neck 124. The opposite end of the cartridge holder 120 defines an annular actuating shoulder 128 positioned adjacent to a second set of external threads 130. The tubular element 122 is sized to receive the cartridge 100 and defines in this embodiment two axially oriented raised lands 132 which are positioned to frictionally engage the collar 106 of the cartridge 100.

The exterior of the tubular element 122 defines a number of features which cooperate with other components of the dispensing device described below. In particular, the tubular element 122 defines a pair of axial grooves 134 which communicate with respective circumferential grooves 136 to form L-shaped grooves that form part of a bayonet mount as described below. The tubular element 122 also defines a pair of stop members 138 which cooperate with a cap as described below. Each of the stop members 138 defines a transverse face 140 and an opposed sloping face 142. The tubular element 122 also defines an annular flange 143 which in turn defines two rearwardly extending stop members 144. A pair of ramps 146 are defined on the exterior of the tubular member 122 near the external threads 130.

Preferably, the cartridge holder 120 is formed of a transparent plastic material such as polycarbonate. This construction allows a user to see the cartridge 100 within the cartridge holder 120 to check the correct insulin and to gauge the amount of medication 110 left in the cartridge 100.

The minimum diameter of the inside of the tubular element 122 is greater than the maximum diameter of the cartridge 100. For this reason, the tubular element 122 receives the cartridge 100 in an easy sliding fit such that the weight of the cartridge 100 will move the cartridge 100 in the tube 122 until the collar 106 contacts the raised lands 132. A slight additional force will push the cartridge 100 to the fully seated position shown in FIG. 8. In this position friction between the lands 132 and the collar 106 will prevent the cartridge 100 from falling out of the holder 120. This arrangement facilitates assembly of the cartridge 100 into the holder 120, because no frictional retarding force is encountered until the cartridge 100 is almost in the fully assembled position. There is therefore, less chance that a user will fail to push the cartridge 100 fully into the holder 120. Furthermore because the cartridge 100 is engaged at the collar 106, it is the diameter of the collar 106 rather than the diameter of the tube 122 that determines the tightness of the friction fit. In many cases, the diameter of the collar 106 can be controlled more closely than the diameter of the glass tube 122, and in these cases this arrangement provides the further advantage of a more consistent fit.

Thus, the lands 132 frictionally engage the collar 106 to releaseably hold the cartridge 100 in the holder 120

and thereby to form a modular unit which can be handled and assembled as a single device. As apparent in FIGS. **2** and **8**, the end of the cartridge **100** that mounts the piston **108** extends out of the cartridge holder **120** for a considerable distance. In this embodiment, that distance is greater than one-half inch. This allows the user to grasp the cartridge **100** when it is necessary to remove the cartridge **100** from the cartridge holder **120** for replacement.

As shown in FIG. **2**, the external threads **126** are sized to mate with internal threads **156** defined by a needle assembly **150**. This needle assembly **150** includes a double-ended hypodermic needle **152** which is mounted to a hub **154** that in turn defines the internal threads **156**. By threading the needle assembly **150** onto the external threads **126** the needle **152** is passed through the central opening **125** and the membrane **104**, into contact with the medication **110**.

As shown in FIGS. **1** and **11–13** the dispensing device includes a removable cap **160** which, when mounted in position, surrounds and protects the needle assembly **150** (if mounted), the cartridge holder **120**, and the cartridge **100**. This cap **160** defines a pair of internal lugs **162** sized to fit within the grooves **134**, **136** to form a bayonet mount in order to hold the cap **160** securely in position on the cartridge holder **120**. In addition, the cap **160** defines a pair of protruding elements **164** positioned to interact with the stop members **138**. When the cap **160** is rotated in a first locking direction, the protruding elements **164** engage the transverse faces **140**, thereby defining a stop position. This allows the cap **160** to be used as a tool to apply torque to screw the cartridge holder **120** into place on the dispensing device without overtightening the bayonet mount. When the cap **160** is rotated in a second unlocking direction, the protruding elements engage the sloping faces **140** to shift the cap **160** axially. The cap **160** can if desired define a clip **166** to retain the dispensing device in a pocket of the user.

As shown in FIGS. **2** and **9** the cartridge holder **120** mounts in the dispensing device by screwing the external threads **130** into a collar **2***b* defined by the dispensing device. This collar **2***b* defines internal threads **176** which mate with the external threads **130**. In addition the collar **2***b* defines elements which cooperate with the stop members **144** and the ramps **146** to define the fully assembled position of the cartridge holder **120** and to hold it in that position. In particular, the collar **2***b* defines a pair of spiral grooves **170**, each of which terminates in a transverse face **172**. When the cartridge holder **120** is threaded into the collar **2***b* the stop members **144** enter the spiral grooves **170**. The faces **172** prevent overtightening of the cartridge holder **120** in the collar **2***b*. The collar **2***b* defines ramps **174** which cooperate with the ramps **146** to define a detent that tends to hold the cartridge holder **120** in the fully assembled position (FIG. **10**).

As best shown in FIG. **2**, when the cartridge holder **120** is assembled in the collar **2***b* the rear end of the cartridge **100** is unrestrained. This arrangement provides particular advantages, because the overall length of the cartridge **100** is difficult to control with conventional manufacturing processes, as explained above. This embodiment accommodates varying lengths of the cartridge **100** because the rear rim of the cartridge body **102** does not contact the dispensing unit. In order to prevent the cartridge **100** from moving undesirably after the cartridge holder **120** has been threaded into the collar **2***b*, the cartridge **100** is restrained from movement by the frictional fit with the raised lands **132** described above.

As described in greater detail below, the dispensing device includes a plunger **5** that is advanced against the piston **108** to dispense the medication **110** through the needle **152**.

The movement of this plunger **5** is controlled in part by a one-way mechanism that allows the plunger **5** to advance but not to retract as long as the cartridge holder **120** is mounted to the collar **2***b*. However, when the cartridge holder **120** is removed from the collar **2***b* to replace the cartridge **100**, this one-way mechanism is released, to allow the plunger **5** to be retracted into the dispensing unit. The details of operation of this one-way mechanism and the manner in which this mechanism is released are explained in detail below in conjunction with FIGS. **14** and **15**. Here, it is enough to note that the one-way mechanism is controlled by the axial position of a member **64** which is slidably mounted in the collar **2***b*. This member **64** abuts the actuating shoulder **128** of the cartridge holder **120** and is shifted rearwardly to engage the one-way mechanism with the plunger **5** when the cartridge holder **120** is mounted in place in the collar **2***b*.

It is the actuating shoulder **128** rather than any part of the cartridge **100** that determines the position of the one-way mechanism actuating member **64**. The cartridge holder **120** can readily be manufactured to high accuracy with conventional molding techniques, and for this reason the actuating shoulder **128** can be precisely positioned to ensure that the member **64** is depressed at the proper instant, just before the cartridge holder **120** is fully assembled into the collar **2***b*. This ensures that there is no substantial movement of the cartridge holder **120** or the cartridge **100** after the one-way mechanism is engaged. This prevents the plunger **5** from exerting undue forces on the piston **108** and minimizes the unintended discharge of medication **110** when the needle **152** pierces the membrane **104**.

Further details of the one-way mechanism, and the operation of the actuating member **64**, as well as the advancing mechanism for the plunger **5** will now be described in conjunction with FIGS. **14** and **15**.

As shown in highly schematic form in FIG. **14** and as discussed above, the cartridge **100** is housed in the housing **120** which is screw fit into the collar **2***b* extending axially from the front end of the dispensing unit.

The dispensing device is provided with a pawl type one-way mechanism which engages teeth on the plunger **5** so as to prevent rearward movement of the plunger **5** once the housing **120** is in place. This one-way mechanism is shown at **60** in FIGS. **14** and **15** and is biassed to retract radially when the cartridge housing **120** is removed. For example, the housing can incorporate a twist mechanism which both locks the cartridge housing in position and actuates the one-way mechanism; or the shoulder **128** of the cartridge housing **120** can bear against part of the one-way mechanism as it seats home to actuate the one-way mechanism. The one-way mechanism disengages when the cartridge housing **120** is removed to allow the plunger **5** to be retracted into the device to permit a new cartridge **100** to be mounted on the dispensing device.

A preferred form of the one-way mechanism is shown in FIG. **14** and comprises a pair of diametrically opposed pawls **60** carried on spring arms **61** snap fitted onto an annular shoulder **20** to extend forward of the

shoulder into the axial socket in which the cartridge 100 is received. The pawls 60 have an inclined rearward face 62 which bears against a correspondingly angled face carried by a collet 63 mounted around the plunger shank and radially inward of arms 61. The collet is attached to a spring loaded sleeve 64 which is a slideable fit within the socket and is spring biassed into its forward position. The front end of the sleeve 64 provides a stop 65 against which the shoulder 128 of the housing 120 bears as it is mounted in the device. This causes the sleeve 64 to be moved axially rearwardly to carry the inclined face of collet 63 clear of the inclined face 62 of the pawl and to bring the rear edge of collet 63 into contact with a stop 67 carried on the radially inward face of arm 61. This causes the arm 61 to flex radially inward and urge pawl 60 into engagement with the teeth on the plunger 5. When the housing 120 is removed to fit a new cartridge 100, this allows the sleeve 64 to move forward under the thrust of the spring so that collet 63 moves forward of release stop 67 and bears against the inclined face 62 to lift the pawl 60 clear of the teeth on the plunger 5. The plunger 5 can now be retracted into the device to enable another cartridge 100 to be fitted. By using the rear of the accurately molded housing 120 to actuate the pawl mechanism 60–67, rather than the rim of the cartridge 100, variations in the size of the cartridge 100 can be accommodated.

Rearwardly of shoulder 20, the body of the device houses the plunger drive mechanism, the means for engaging and disengaging the drive mechanism from the plunger, and the dosage selection means. In the form of the device shown, these take the form of a series of members concentrically journalled around the plunger 5.

As shown the housing comprises a rotatable section 6 which houses the drive engagement mechanism; a fixed section 7 containing the dosage selection mechanism and having a port 8 through which a scale 9 indicating the dose selected can be seen by the user; a further rotatable collar or sleeve 10 for operating the dosage selection mechanism: and a terminal axially operating push button 11 for driving the plunger 5 forward to dispense the selected dose. The various sections of the housing can have any desired external shape, but it is preferred that the housing 1, sleeve 6 and section 7 have an oval external cross-section so that the relative rotational position of one with respect to the other can readily be detected by a user, notably by a blind person.

The plunger 5 preferably has a substantially circular cross-section but can have a squared, triangular or other cross-section shape if desired. For example, as shown in FIG. 15, it may have two opposed flats along its length to guide the drive means.

The plunger 5 carries a series of circumferential ribs or teeth 22 which form an axial ratchet into which the one-way mechanism 21 and the radially clampable drive mechanism described below engage. The teeth 22 are of a saw tooth form with a scarp face of the teeth directed rearwardly. Preferably, the teeth extend axially for the full length of the plunger 5. It is preferred that the axial distance from one tooth to the next corresponds to a dosage unit for the material being dispensed.

Located to the rear of shoulder 20 is the drive mechanism and the mechanism for engaging and disengaging this from the plunger. The drive mechanism is a pawl type mechanism which is radially engageable and disengageable with the teeth on the plunger and comprises two jaws 23 and 24 diametrically opposed to one another and carrying on their radially inward faces teeth which correspond to and engage with the teeth 22 on the plunger.

The jaws are normally urged radially outwardly, as shown for jaw 24 in FIG. 14, by transverse coil springs acting between the jaws 23 and 24 or by other bias means (not shown) so that their teeth do not engage those of the plunger which is then free to move axially with respect to the jaws when they are in their outward position, but is locked to the jaws when they are in their radially inward position, as shown for jaw 23 in FIG. 14.

The jaws are moved radially inward against the thrust of the coil springs by a pair of cams carried on the internal face of the rotatable section 6 of the housing or formed by the narrower diameter sectors of the oval cross-section of the rotatable section 6. The user has to twist section 6 to engage or disengage the jaws from plunger 5 and thus engage or disengage the drive to the plunger. If desired, section 6 can be spring biassed towards the drive disengaging position so that the user always has to twist section 6 before the device can be used.

The shoulder 20, as shown in FIG. 14, defines the forward limit of the travel of the drive mechanism and provides the datum point from which the dosage is determined. In the device shown in FIGS. 14 and 15 the forward faces of jaws 23 and 24 butt against the rear face of shoulder 20 to set the zero or datum point for the dosage selection mechanism.

A push sleeve 25 journalled on plunger 5 and within the dosage selection mechanism described below acts axially on the rear faces of the jaws 23 and 24 when in their drive engaged position to drive the jaws and hence the plunger 5 forward. When the jaws are in the drive disengaged position, they still bear against the push sleeve so that they carry it axially rearwards with them during the dosage selection. The push sleeve 25 provides the mechanical link between the terminal push button 11 which a user presses and the jaws 23 and 24.

The jaws 23 and 24 are moved axially by means of a split jaw drive sleeve 26 which has forward hooks 27 which engage similar recesses 28 at the rear of the jaws and rearward hooks 29 or other flexible linkages which connect the sleeve 26 axially to the forward end of the screw sleeve 30 of the dosage selection mechanism. When the jaws are in the drive disengaged position as shown for jaw 24 in FIG. 14 the hooks 27 and recesses 28 are engaged and the jaws can be moved axially with the screw sleeve 30. When the jaws are in the drive engaged position, as shown for jaw 23 in FIG. 14, the hooks 27 are released from recesses 28 to permit the jaws to move axially with sleeve 25 and free from the screw sleeve 30.

The dosage selection mechanism is housed within section 7 of the housing and comprises a screw sleeve 30 journalled for rotation and axial movement upon push sleeve 25. Sleeve 30 carries an external screw thread 31 which engages a similar thread 32 carried internally by section 7 of the body of the device. Sleeve 30 is rotated and thus caused to move axially by means of a collar driving the sleeve through a spined drive 33 shown in FIG. 15. The window insert in port 8 preferably has a ratchet or clicker mechanism 34 to give an audible indication as the dose is selected.

Retraction of sleeve 30 carries the jaw drive sleeve 26 and the jaws 23 and 24 with it when they are in the

disengaged position and the dose selected can be seen through port 8. Re-engagement of jaws 23 and 24 with the plunger breaks the latch 27/28 and allows the push sleeve 25 and the jaws 23 and 24 to move independently of the screw sleeve 30 and the jaw drive sleeve 26.

To indicate when there is insufficient fluid left in the cartridge to achieve the next dose, a radial shoulder or stop 50 is located at or adjacent the rearward end of plunger 5. This co-operates with a corresponding stop or shoulder 51 at the forward end of the push sleeve 25. The stops engage when the push sleeve is retracted to the maximum extent possible as the plunger 5 approaches the extreme of its forward travel. The user can then see from the dose displayed at the port 8 whether the cartridge contains the requisite amount of fluid. Since the plunger drive is not engaged at this time, the user can then set the dosage mechanism to the required dose if this is less than the amount indicated as remaining in the cartridge without having to discharge fluid as with a conventional device.

Push sleeve 25 is provided with a push button end cap 11 protruding axially from the body of the device which the user depresses to drive the sleeve 25 forward within the housing until the front face of jaws 23 and 24 butt against the rear of shoulder 20. The jaws 23 and 24 can only be moved rearwardly when they have been disengaged from the teeth 22 on the plunger 5, since the one-way mechanism will prevent rearward movement of the plunger 5. If a user attempts to set the dosage mechanism while the drive is engaged, he will detect resistance to rotation of sleeve 10. If he ignores this, the spline drive 33 between collar 10 and the screw sleeve 30 will be over-ridden to release the screw sleeve to prevent damage to the mechanism. However, unless the drive is engaged, depression of button 11 will not achieve any forward movement of the jaws or discharge of fluid from the cartridge 100.

The above device can be manufactured in many suitable materials and readily lends itself to manufacture by injection molding of suitable plastics materials with the various components being snap fits upon one another.

In operation, a user initially prepares the dispensing device for use by removing the holder 120, inserting a cartridge 100 in the holder 120, and then screwing the holder 120 into place on the collar 2b. The needle assembly 150 is then screwed into place on the housing 120. The user then rotates the sleeve 6 to disengage the drive mechanism if this has not already been done. Jaws 23 and 24 should be seated against the rear face of shoulder 20, the zero setting, from the previous use of the device, but the screw sleeve 30 will be at the dosage position previously selected. The user can thus see what dose was last administered where a sequence of different doses has to be administered. Collar 10 is rotated, say clockwise, to bring sleeve 30 to its forward position at which the latching mechanism 27/28 engages the jaws 23 and 24 and seats them firmly against the rear face of stop 20. The engagement of the latches can be used to provide an audible signal when this occurs, or the resistance to further forward movement will provide the signal to the user that the zero setting has been reached. The dosage displayed through port 8 will now read zero.

Collar 10 is then rotated counter-clockwise the desired number of turns, as evidenced by the number of clicks heard or by the dose displayed at the port 8, to retract screw sleeve 30, the jaw drive sleeve 26 and the jaws 23 and 24 and the push sleeve 25 the desired distance with respect to plunger 5. This will also cause the push button 11 to be extended from the rear end of the device. If the user inadvertently turns the collar 10 too far, it can be rotated clockwise to the correct position without moving the plunger.

Sleeve 6 is then rotated to re-engage the positive drive between the push sleeve 25, the jaws 23 and 24 and the plunger 5. This action will also disengage the latch 27/28 between jaws 23 and 24 and the jaw drive sleeve 26. At this point the device is cocked and ready to dispense the desired dose from the cartridge. However, the device has required a series of positive actions to achieve this state and would not normally be retained by a user in the cocked state, but would be stored with the drive disengaged so that accidental actuation of the device can not occur.

The user then inserts the point of needle 3 into his arm, buttock or other suitable point in his body and depresses button 11 to administer the dose of insulin. The dose is administered by depressing the button fully. If the button is not depressed fully, the user can detect this and can complete the dose administration. If desired, a colored band can be mounted around button 11 which will remain partially exposed until the button is fully depressed. Release of pressure on button 11 does not allow the plunger 5 to retract as with previous designs, so that jerky or interrupted depression of button 11 does not allow the user to pump the device to administer an excessive dose.

When the full dose has been administered, the jaws 23 and 24 will butt against the rear of shoulder 20. Due to the action of the one-way mechanism 21, 60–67, the blocks 23 and 24 cannot be retracted and administration of a further dose of insulin is not possible until the whole process of dose selection and re-cocking of the device is carried out. The device will therefore resist accidental overdosing due to repeated pressing of button 11.

As stated above, the cartridge-holder assembly of this invention finds use wherever it is desired to provide a removable cartridge for a measured dose syringe, for example in the administration of other medicaments or in dispensing accurately known amounts of a fluid, for example in blood tests or analytical work. It will also be appreciated that the assembly may be altered in ways which do not affect the fundamental operating concept of the assembly, for example by using other materials and configurations.

It is therefore intended that the foregoing detailed description be regarded as illustrative rather than limiting, and that it be understood that it is the following claims, including all equivalents, which are intended to define the scope of this invention.

I claim:

1. A cartridge assembly for a syringe-type medication dispensing unit, said assembly comprising:

a cartridge comprising a cartridge body having first and second ends, a pierceable membrane mounted at the first end, and a piston mounted at the second end, with a volume of mediation contained in the cartridge body between the membrane and the piston;

a cartridge holder having first and second ends, said first holder end defining a central opening and means for mounting a double ended needle, said second holder end defining means for securing the holder to a medication dispensing unit and an actuating shoulder, said holder defining a central cavity;

one of said central cavity and said cartridge being shaped with a plurality of raised lands adapted to frictionally to engage the opposed surface of the other of said cartridge and cavity so as to form an assembly which can be handled as a single modular unit with the cartridge held securely in the holder.

2. The invention of claim 1 wherein the double ended needle mounting means comprises a first set of external threads.

3. The invention of claim 1 wherein the holder securing means comprises a second set of external threads.

4. A cartridge assembly for a syringe-type medication dispensing unit, said assembly comprising:

a cartridge comprising a cartridge body having first and second ends, a pierceable membrane mounted at the first end, and a piston mounted at the second end, with a volume of medication contained in the cartridge body between the membrane and the piston;

a cartridge holder having first and second ends, said first holder end defining a central opening and means for mounting a double ended needle, said second holder end defining means for securing the holder to a medication dispensing unit and an actuating shoulder, said holder defining a central cavity shaped to receive and frictionally engage the cartridge to form an assembly which can be handled as a single, modular unit with the cartridge held securely in the holder;

wherein the holder securing means comprises a second set of external threads; and

wherein the modular unit is mounted to a syringe type medication dispensing unit having a plunger engageable with the piston, a one-way mechanism engaged with the plunger, and an actuating member for the one-way mechanism, wherein the second holder end is received within the dispensing unit, wherein the second set of external threads is engaged with the dispensing unit, and wherein the actuating shoulder is engaged with the actuating member.

5. The invention of claim 4 wherein the dispensing unit and the holder define a detent system which holds the second set of external threads in engagement with the dispensing unit.

6. The invention of claim 5 wherein the detent system comprises inter engaging ramps on the holder and the dispensing device adjacent the second set of external threads.

7. The invention of claim 1 wherein the modular unit is mounted to a cap which encloses the first end of the holder, wherein the holder defines at least one stop member wherein the cap defines at least one lug, wherein at least one of the stop member and lug has a transverse face and a sloping face oriented such that the stop member and lug abut at the transverse face to limit rotation of the cap when the cap is rotated in a first direction with respect to the holder, and the stop member and the lug abut at the sloping face to shift the cap axially along the holder when the cap is rotated in a second direction with respect to the holder.

8. The invention of claim 1 wherein the modular unit is mounted to a cap which encloses the first end of the holder; wherein one of the holder and the cap defines at least one groove having an axial portion and a circumferential portion; and wherein the other of the holder and the cap defines a protruding element shaped to slide in the groove to secure the cap and holder together in a bayonet mount.

9. The invention of claim 1 wherein the holder frictionally engages only the first end of the cartridge.

10. The invention of claim 9 wherein the cartridge defines an annular collar disposed around the membrane, and wherein the holder frictionally engages the cartridge only at the collar.

11. The invention of claim 10 wherein the plurality of raised lands are positioned on the holder to frictionally engage the collar.

12. The invention of claim 2 further comprising:

a needle assembly comprising a double ended needle secured to a mounting element which defines a set of internal threads engaged with the first set of external threads of the holder, with one end of the needle passing through the membrane and in contact with the medication.

13. The invention of claim 1 wherein the medication comprises an insulin solution.

14. The invention of claim 1 wherein the second end of the cartridge extends out of the holder by a distance of about ½ inch or more.

15. A cartridge assembly for a syringe-type medication dispensing unit, said assembly comprising:

a cartridge comprising a cartridge body having first and second ends, a pierceable membrane mounted at the first end, and a piston mounted at the second end, with a volume of medication contained in the cartridge body between the membrane and the piston and an annular collar disposed around the membrane;

a cartridge holder having first and second ends, said first holder end defining a central opening and a first set of external threads, said second holder end defining an actuating shoulder and a second set of external threads said holder defining a central cavity shaped to receive the cartridge with the pierceable membrane adjacent the central opening, said cartridge having a length greater than that of the holder such that the second end of the cartridge extends out of the holder,

said holder defining a plurality of raised lands positioned to frictionally engage the collar to form an assembly which can be handled as a single, modular unit with the cartridge held removably in the holder by friction between the collar and the holder, said holder shaped to receive the cartridge freely until the lands engage the collar, such that the weight of the cartridge will move the cartridge into the holder until the lands contact the collar.

16. The invention of claim 15 wherein the modular unit is mounted to a syringe type medication dispensing unit having a plunger engageable with the piston, a one-way mechanism engaged with the plunger, and a one-way mechanism actuating member, wherein the second hold end is received within the dispensing unit, wherein the second set of external threads is engaged with the dispensing unit, and wherein the actuating shoulder is engaged with the one-way mechanism actuating member.

17. The invention of claim 16 wherein the dispensing unit and the holder define a detent system which the second set of external threads in engagement with the dispensing unit.

18. The invention of claim 17 wherein the detent system comprises inter-engaging ramps on the holder

and the dispensing device adjacent the second set of external threads.

19. The invention of claim **18** wherein the modular unit is mounted to a cap which encloses the first end of the holder, wherein the holder defines at least one stop member, wherein the cap defines at least one lug, wherein at least one of the stop member and lug has a transverse face and a sloping face oriented such that the stop member and lug abut at the transverse face to limit rotation of the cap when the cap is rotated in a first direction with respect to the holder, and the stop member and the lug abut at the sloping face to shift the cap axially along the holder when the cap is rotated in a second direction with respect to the holder.

20. The invention of claim **15** wherein the modular unit is mounted to a cap which encloses the first end of the holder; wherein one of the holder and the cap defines at least one groove having an axial portion and a circumferential portion; and wherein the other of the holder and the cap defines a protruding element shaped to slide in the groove to secure the cap and holder together in a bayonet mount.

21. The invention of claim **15** further comprising:

a needle assembly comprising a double ended needle secured to amounting element which defines a set of internal threads engaged with the first set of external threades of the holder, with one end of the needle passing through the membrane and in contact with the medication.

22. The invention of claim **15** wherein the medication comprises insulin.

23. The invention of claim **15** wherein the lands are axially oriented.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 4,936,833

DATED : June 26, 1990

INVENTOR(S) : Bernard Sams

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE CLAIMS

Col. 10, line 59, claim 1, delete "mediation" and substitute therefor --medication--;

Col. 12, line 58, claim 16, delete "hold" and substitute therefor --holder--.

Col. 12, line 64, claim 17, after "which" insert --holds--.

Col. 14, line 8, claim 21, delete "amounting" and substitute therefor --a mounting--.

Col. 14, line 10, claim 21, delete "threades" and substitute therefor --threads--.

Signed and Sealed this

Twenty-second Day of December, 1992

Attest:

Attesting Officer

DOUGLAS B. COMER

Acting Commissioner of Patents and Trademarks

EXHIBIT 20

US006004297A

United States Patent [19]

Steenfeldt-Jensen et al.

[11] **Patent Number: 6,004,297**

[45] **Date of Patent: Dec. 21, 1999**

[54] **INJECTION SYRINGE**

[75] Inventors: **Søren Steenfeldt-Jensen**, Hornbæk; **Steffen Hansen**, Hillerød, both of Denmark

[73] Assignee: **Novo Nordisk A/S**, Bagsvaerd, Denmark

[21] Appl. No.: **09/238,849**

[22] Filed: **Jan. 28, 1999**

Related U.S. Application Data

[60] Provisional application No. 60/073,820, Feb. 5, 1998.

[30] **Foreign Application Priority Data**

Jan. 30, 1998 [DK] Denmark 00130/98

[51] **Int. Cl.**[6] **A61M 5/00**

[52] **U.S. Cl.** **604/207**; 604/211

[58] **Field of Search** 604/207, 208, 604/211, 218, 232

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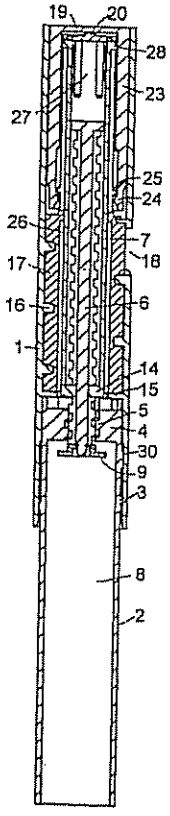
Primary Examiner—John D. Yasko
Attorney, Agent, or Firm—Steve T. Zelson, Esq.

[57] **ABSTRACT**

An injection syringe comprises a housing (1), a piston rod (6) with a non-circular cross-section and an outer thread (7), a piston rod drive which includes a piston rod guide (85) mating with the cross-section of the piston rod (6), and a nut (4) which is not axially displaceable and which mates with the thread (7) of the piston rod (6) to form a self-locking thread connection. Rotation of a dose setting element (81) causes an injection button to be screwed out to project from the housing (1). When the injection button (88) is pushed axially, such axial movement is transformed, by way of the threaded coupling, into a rotation of one of the piston drive elements (85) relative to the other one (4). A unidirectional coupling between the nut member (4) and the piston rod guide (85) allows rotation in one direction by which the piston rod (6) is transported in a distal direction. The coupling has an initial reluctance to be overcome before rotation takes place, said reluctance being large enough to resist torques exerted during the dose setting.

8 Claims, 5 Drawing Sheets



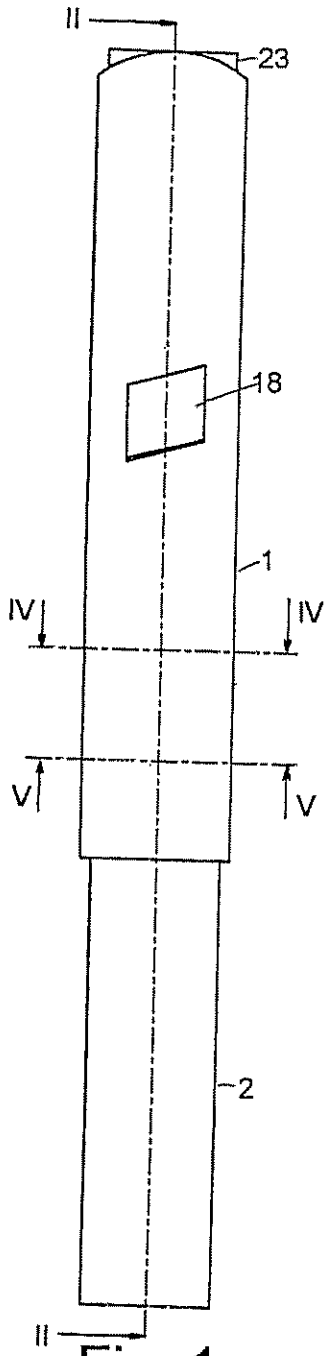


Fig. 1

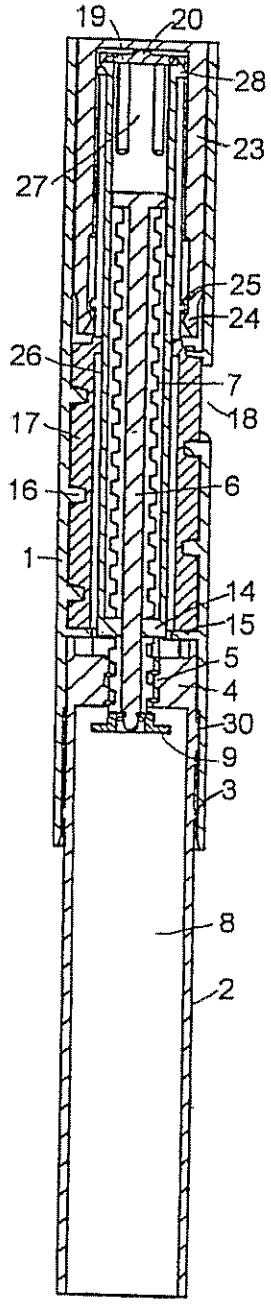


Fig.2

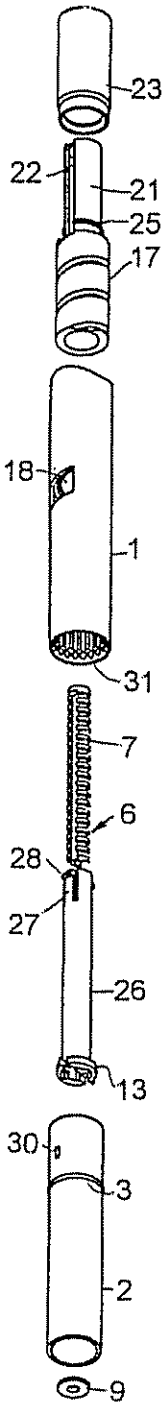


Fig.3

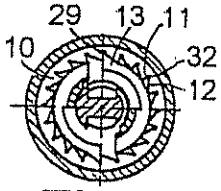


Fig.4

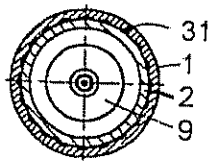


Fig. 5

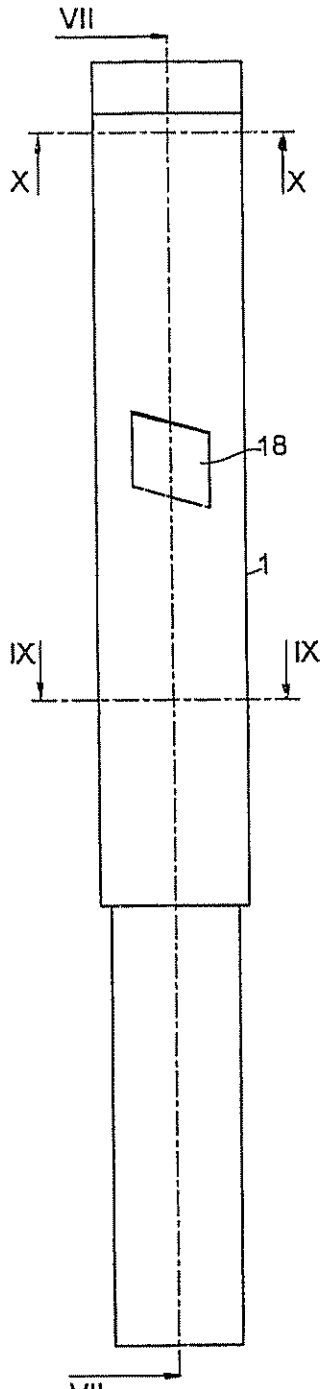


Fig. 6

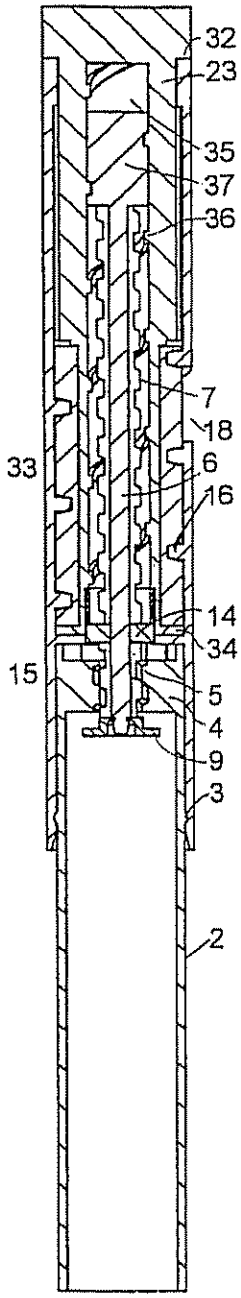


Fig. 7

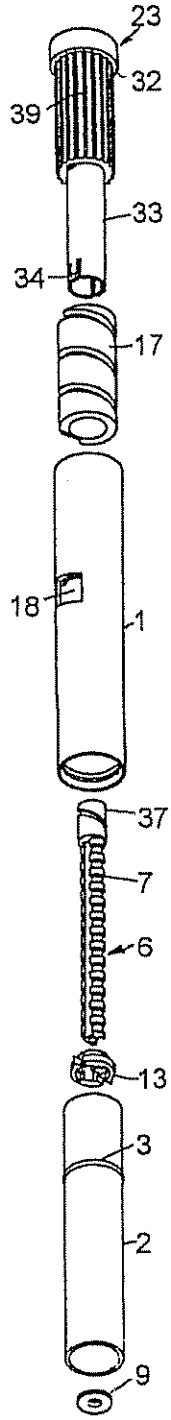


Fig.8

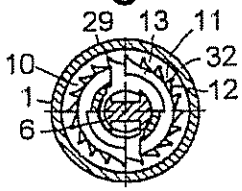


Fig. 9

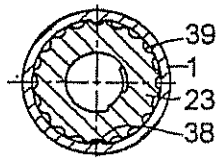


Fig.10

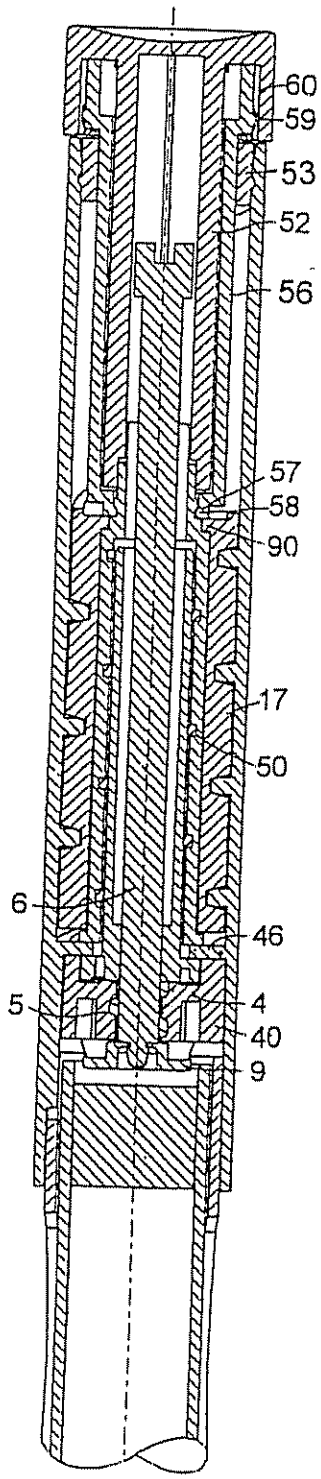


Fig. 11

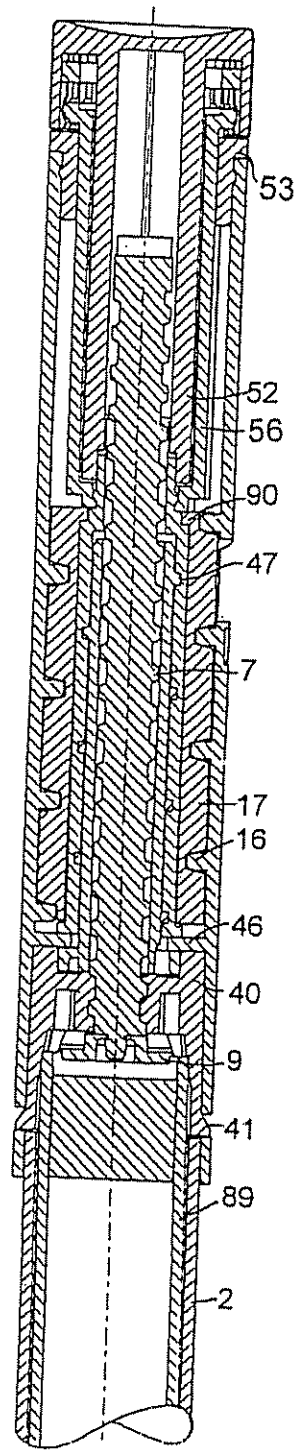


Fig. 12

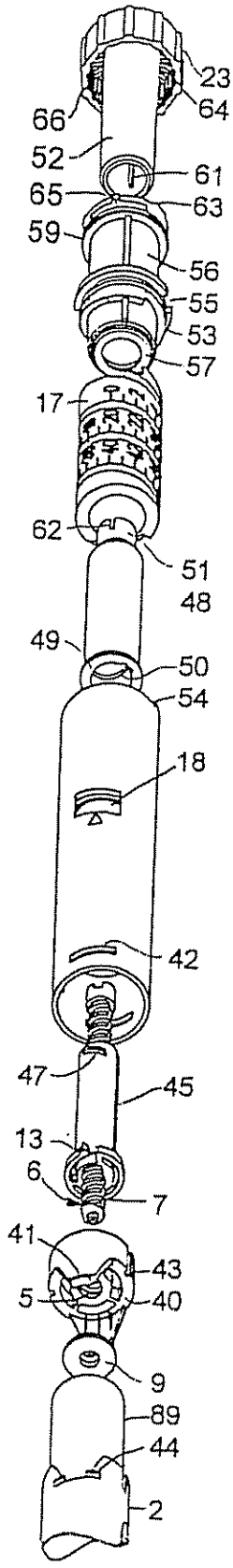


Fig. 13

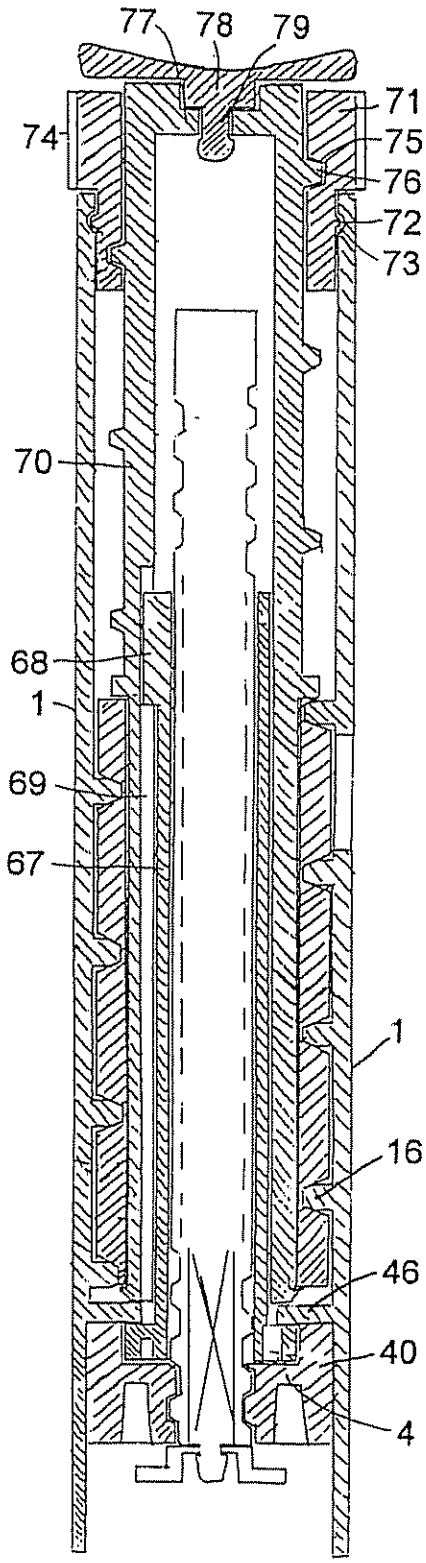


Fig. 14

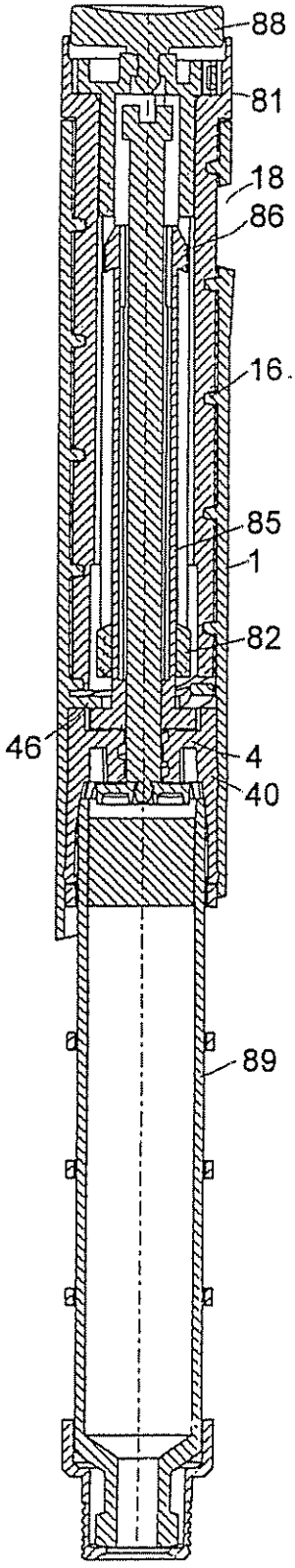


Fig. 15

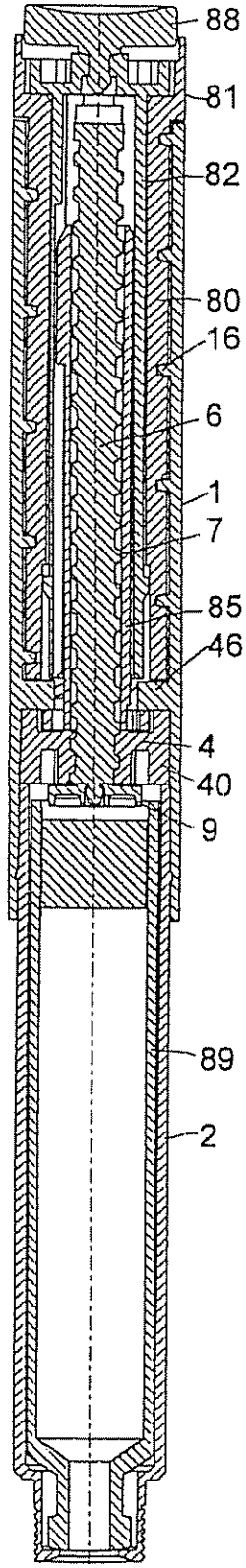


Fig. 16

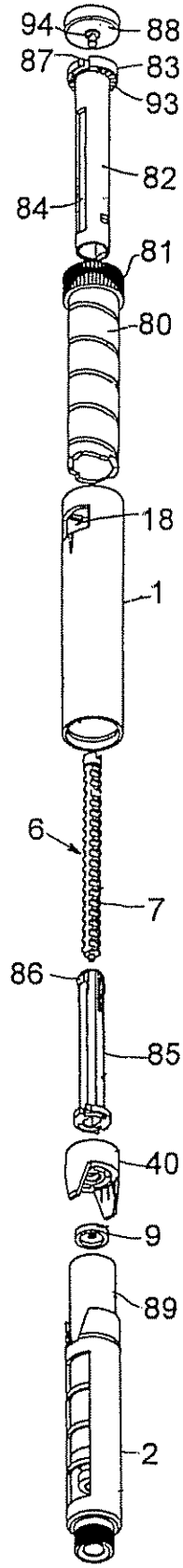


Fig. 17

INJECTION SYRINGE

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority under 35 U.S.C. 119 of Danish application PA 1998 00130 filed Jan. 30, 1998 and of U.S. provisional no. 60/073,820 filed Feb. 5, 1998, the contents of which are fully incorporated herein by reference.

The invention relates to injection syringes of the kind apportioning set doses of a medicine from a cartridge containing an amount of medicine sufficient for the preparation of a number of therapeutic doses.

Such syringes are mainly made for users who have to inject themselves frequently, e.g. diabetics. A number of demands are set to such syringes. The setting of a dose must be easy an unambiguous and it must be easy to read the set dose. It must be possible with a minimum of trouble to cancel or change a wrongly set dose and when the dose is injected the dose setting must return to zero. When a disposable syringe is in question, i.e. a syringe which is disposed of when the cartridge is empty, the syringe must further be cheap and made of materials suited for recycling or burning without producing noxious gases. For these purposes the number of parts from which the syringe is constructed and the number of different kinds of materials used in the syringe should be kept at a minimum.

Most dose setting devices work with a threaded piston rod co-operating with a nut where the nut and the piston rod may be rotated relative to each other. The dose setting may be obtained by screwing the nut away from a stop to which it is returned during the injection by pressing the piston rod until the nut member abuts the stop. By other dose setting devices one of the elements, the nut or the piston rod, is kept inrotatable and the other is allowed to rotate a set angle depending on the set dose, whereby the piston rod is screwed a distance through the nut.

In most syringes for apportioning set doses it is preferred that the piston rod is backing up the piston upon which it works during the injection. To obtain this precaution is taken to prevent the piston rod from moving in a proximal direction.

The syringe according to EP 327 910 is of the type wherein a nut is screwed away from a stop. During the setting of the dose the screwing may be performed in both direction so that a too large set dose may be lowered just by rotating the nut in an opposite direction. Means are provided preventing that negative doses are set. The mutual rotation of the piston rod and the nut is obtained by rotating a cap relative to the pen housing and a set dose may be read on a scale and a pointer provided at adjacent edges of the housing and the cap, these edges being so shaped that the cap can only be mounted firmly on the housing when the pointer points zero on the scale. It may be seen as a weak point that doses larger than the one obtained by rotating the parts 360° must be calculated by adding the number pointed at on the scale and a number printed on the side of a tubular extension of the nut which is moved out from the proximal end of the housing proportionally with the dose set and which tubular extension is closed at its proximal end to form an injection button.

In EP 450 905 the above drawback is overcome by writing the numbers along a helical line on a tubular extension of the nut so that these number may successively be seen in a window in a housing element enclosing said tubular extension. Hereby the size of the dose is indicated unambiguously but the user have to remember to set the dose setting device on zero before the next setting of a dose is performed. If this is forgotten a wrong dose may be set and the number may not be seen clearly in the window.

In EP 608 343 is described a pen having a dose setting mechanism wherein the dose is set by rotating a button relative to a housing to set a dose. By the rotation the button is screwed up from the end of the housing in a thread having a pitch so large that the thread connection is not self blocking, i.e. when the button is presses back to the end of the housing it will rotate back in the thread. The button is through a ratchet coupled to a driver, the ratchet forming a unidirectional coupling which during the rotation of the button in one direction to set a dose rides or clicks over the teeth of the ratchet. The cylindrical side of the button carries numbers which shows the size of the set dose in a window when the button is screwed outward. When the button is screwed back the unidirectional coupling will transmit the rotation to the driver which has a nut co-operating with a threaded piston rod which is made inrotatable in a housing. This thread connection has a pitch which makes the nut self locking on the piston rod. A set dose may be cancelled by drawing the engaging parts of the ratchet out of engagement against the force of a spring so that the rotation of the button is not transmitted to the driver and then press the button back to the housing. This pen fulfils all the objects mentioned only the dose cancelling procedure is a little troublesome as the dose set button cannot as it will come most naturally just be screwed back if a too large dose is set. Concomitantly forcing the coupling parts apart against the force of the spring and pressing or screwing the button back may be a little difficult and the demand for a spring necessitates use of metal parts in the syringe.

It is an object of the invention to provide a syringe which has the mentioned advantageous features without having the drawbacks known from existing syringes.

This is obtained by an injection syringes for apportioning set doses of a medicine from a cartridge containing an amount of medicine sufficient for the preparation of a number of therapeutic doses, comprising

- a housing
- a piston rod having a not circular cross-section and an outer thread
- a piston rod drive comprising two elements
  - a) a piston rod guide in relation to which the piston rod is axially displaceable but not rotatable, and
  - b) a nut member which is rotatable but not axially displaceable in the housing and which has an inner thread mating the thread of the piston rod to form a self locking thread connection,
- a dose setting mechanism comprising a not self locking thread connection along which an injection button by rotation of a dose setting element relative to said housing is screwed out from the proximal end of the housing to project from this proximal end a distance determined by the angle of said rotation and which thread connection by axial returning of the injection button transforms this axial movement to a rotation of one of the piston drive elements relative to the other,

which syringe according to the invention is characterised in that

- a unidirectional coupling is provided between the nut member and the piston rod guide allowing rotation of these parts relative to each other in one direction but not in the opposite direction, the allowed rotation being one by which the piston rod is transported in a distal direction in the syringe, the coupling being so designed

that a set initial reluctance has to be overcome before the rotation takes place.

During the setting of a dose a torque is exerted on the unidirectional coupling in the direction in which this coupling allows rotation after a set initial reluctance has been overcome. As this torque is a weak one resulting when the male and the female part of a not self locking thread connection is rotated relative to each other the initial reluctance can be made large enough to allow this rotation without causing any relative rotation of the parts in the coupling.

When the injection button is pressed the movement of this button is transformed into a rotation of the piston rod (or the nut member) relative to the nut member (or the piston rod). When the button is pressed hard enough the initial reluctans is overcome so that the two elements, the piston rod and the nut member, are rotated relative to each other.

According to the invention a click coupling providing an moderate resistance against rotation is established between the housing and the element rotated relative to the housing to set a dose. Hereby it is ensured that the position corresponding to a set dose is maintained and is not inadvertently altered. The clicks may be taken as an audible signal indicating the size of the set dose.

The unidirectional coupling may be a coupling comprising a pawl sliding over a pawl wheel with teeth having a steep front edge and a ramp shaped trailing edge, and the initial reluctance may be obtained by the fact that the trailing edges of the pawl wheel teeth has a depression engaged by a mating protrusion on the pawl.

A dose scale drum which has in its surface a helical track engaged by a helical rib on the inner side of the housing to form a not self locking thread connection between the housing and the drum may be coupled to the injection button to be moved axially with this button. This way the dose scale drum will be rotated relative to the housing when it is axially displaced with the injection button in said housing.

The thread connection by which the injection button is screwed out from the housing by setting a dose may be the thread connection between the dose scale drum and the housing. In this case the dose scale drum must be coupled to a driver rotating the piston rod (or the nut member) relative to the nut member (or the piston rod) when the injection button is pressed.

A dose is set by rotating an element relative to the housing, and this element may be an element carrying the nut member and the unidirectional coupling so that the rotation is transmitted through said unidirectional coupling to the dose setting drum. The rotation transmitted is in the direction in which the coupling can run free when an initial reluctance is overcome. However, the force needed to screw the dose scale drum up along its thread is not large enough to overcome said reluctance and consequently the rotation is transmitted through the coupling.

In one embodiment of the syringe according to the invention the element rotated relative to the housing may be a part carrying the nut member and the unidirectional coupling through which the rotation is transmitted to the dose setting drum.

In another embodiment of the syringe according to the invention the element rotated relative to the housing may be the injection button and the not self locking thread connection which determines the lifting of the injection button may be an inner thread in a bore in the injection button engaging an outer thread on an enlargement of the piston rod. When the injection button is screwed up along the piston rod to project from the housing a torque is exerted on the piston rod trying to rotate this piston rod in a direction which will move it in a distal direction in the syringe. Such a rotation is just the rotation which is allowed by the uniderectional coupling which blocks rotation in the opposite direction. Due to the initial reluctance against rotation of the coupling parts relative to each other the piston rod will not be rotated when the injection button is screwed up along it in a proximal direction in the syringe. If the injection button is screwed in the opposite direction the unidirectional coupling will definitively block a relative rotation of the piston rod and the nut member in the direction which would draw the piston rod in a proximal direction.

In the last mentioned embodiment of the injection syringe the dose scale drum may b e mounted rotateable but not axially displaceable on the injection button. When the dose scale drum is moved with the injection button in the axial direction of the syringe the drum will be rotated due to the not self locking thread connection between said drum and the housing so that a number on the drum corresponding to the set dose is visible in a window provided in the wall of the housing. In this embodiment the pitch of the dose drum thread need not be identical with the pitch of the thread along which the injection button is screwed to set a dose, only both thread connections must have a pitch large enough to make the thread connection the not self locking type, i e. of the type by which an axial movement can be transformed into a rotation.

In an appropriate embodiment of the syringe according to the invention the dose scale drum is mounted rotatable but not axially displaceable on the injection button.

During the injection the injection button must be kept inrotatable but axially displaceable relative to the housing in the angular position to which the injection button is rotated during the setting of a dose. This may be obtained by letting the click coupling between the housing and the injection button comprise protrusions on one part engaging axial grooves in the other. When the injection button is pressed home into the housing the internal thread in the bore of this button will act on the engaging outer thread on the enlargement at the end of the piston rod and convert the axial movement of the injection button to a rotational movement of the piston rod in a direction by which the piston rod is screwed through the nut member in a distal direction in the syringe. The piston rod guide which is connected to one part of the unidirectional coupling is allowed to rotate when the initial reluctance against rotation in the direction else allowed by the coupling is overcome. Also a rotational movement of the dose scale drum is induced by the axial movement of the injection button so that the scale is returned to its zero position when the button is pressed home. When rotation of the dose scale drum and the piston rod is induced by the axial movement of the injection button this button is reacted upon by a torque which must be taken up by the click connection between the injection button and the housing which connection must consequently be strong enough to absorb this force without rotating.

In the following the invention is described in further details with references to the drawing, wherein

FIG. 1 shows a front view of an embodiment of an injection syringe according to the invention,

FIG. 2 shows a sectional view along the line II—II in FIG. 1,

FIG. 3 shows in a reduced scale an exploded view of the syringe in FIG. 1,

FIG. 4 shows a sectional view along the line IV—IV in FIG. 1,

FIG. 5 shows a sectional view along the line V—V in FIG. 1,

FIG. 6 shows a front view of another embodiment of an syringe according to the invention,

FIG. 7 shows a sectional view along the line VII—VII in FIG. 6,

FIG. 8 shows in a reduced scale an exploded view of the syringe in FIG. 6,

FIG. 9 shows a sectional view along the line IX—IX in FIG. 6,

FIG. 10 shows a sectional view along the line X—X in FIG. 6

FIG. 11 shows a sectional side view of another embodiment of a syringe according to the invention,

FIG. 12 shows a sectional side view perpendicular to the view in FIG. 11,

FIG. 13 shows in a reduced scale an exploded view of the syringe in FIGS. 11 and 12,

FIG. 14 shows a sectional side view of the dose setting part of another embodiment of a syringe according to the invention,

FIG. 15 shows a sectional side view of still another embodiment of a syringe according to the invention,

FIG. 16 shows a sectional side view perpendicular to the view in FIG. 15,

FIG. 17 shows in a reduced scale an exploded view of the syringe in FIGS. 15 and 16,

Initially it may be convenient to define that in this application directions of rotation are always seen from the proximal end of the pen and designed as clockwise or anticlockwise seen in this direction.

FIG. 1 shows an injection syringe of the kind by which a liquid from an ampoule can be apportioned in a number of individually set does. FIG. 3 shows an exploded view of this syringe and the FIGS. 2, 4 and 5 sectional views taken along different lines in FIG. 1.

The syringe comprise a tubular housing 1 which is by a partition 15 divided into a first and a second division into the first one of which an ampoule holder 2 is snapped by a snap lock comprising a ring shaped bead 3 on the ampoule holder 2 which bead is snapped into a corresponding circumferantial grove in the inner wall of the housing 1 near an open end thereof. By this snap connection the ampoule holder 2 is secured in the housing 1 so that it can be rotated but not axially displaced relative to this housing.

In the syringe ready for use an ampoule is mounted in the ampoule holder which is then at its distal end closed by an end wall provided with a needle hub receiving part onto which a needle hub can be mounted having a needle with one end communicating with the content of the ampoule and the other end free to be inserted into a patient. In the shown syringe, however, neither ampoule, end wall nor needle hub are shown.

The end of the ampoule holder 2 inserted in the housing 1 is closed by a wall 4 having a central bore with an internal thread 5. A piston rod 6 having an external thread 7 mating the thread 5 of said bore extends through said bore. The threads are so designed that a clockwise rotation of the piston rod will drive this rod into an ampoule accommodating compartment 8 in the first division of the housing 1. At its end projecting into the compartment 8 the piston rod 6 is provided with a pressure foot 9 designed to abut a piston closing the rear end of an ampoule accommodated in the ampoule holder 2.

In the proximal side of the end wall 4 the bore is enlarged and the internal side of the enlargement is provided with pawl wheel teeth 10 having a steep front edge 11 facing the clockwise direction and a ramp shaped rear edge 12 facing the anticlockwise direction. At least one pawl 13 mounted on a piston rod guide 14 co-operates with the pawl teeth 10 so that said piston rod guide can only be rotated clockwise in the ampoule holder 2.

On the inner wall of the second division of the housing 1 a helical protruding rib 16 is provided defining an inner thread with a high pitch. A dose scale drum 17 is in its outer wall provided with a helical grove defining a corresponding external thread mating the inner thread just mentioned. The pitch angle of the threads exceeds the angle of friction for the materials forming the parts of the thread connection and consequently the thread connection is of the not self locking type which induce a relative rotation of the parts of the connection when these part are moved axially relative to each other.

Numbers indicating set doses are printed on the outer wall of the dose drum 17 and the number corresponding to a set dose is shown in a window 18 provided in the side wall of the housing 1.

The dose scale drum 17 is provide with a tubular extension 21 having an end near the proximal end of the syringe. Said end of the extension is closed by an end wall 19 having a central outer protrusion 20. In a part of the wall adjacent to the end wall 19 the extension 21 is provided with slots 22. The said end of the extension is covered by a cup shaped cap 23 forming an injection button. Internal hooks 24 at the open end of this cap snaps over an external circumferential bead 25 on the extension 21 and the protrusion 20 on the end wall 19 abuts the inner side of the bottom of the cap 23 to form a journal about which the injection button can rotate relative to the extension 21 whereas it cannot be axially displaced relative to this extension

A driver tube 26 integral with the piston rod guide 14 extends from this piston rod guide to the end wall 19 of the dose scale drum extension 21 and is at its proximal end divided into tongues 27 terminated by external hooks 28 engaging the slots 22 in the extension 21. This way the dose scale drum 17 is bound to rotate with the driver tube 26 but is axially displaceable relative to this tube.

To set a dose the ampoule holder 2 is rotated anticlockwise in the first division of the housing 1. This rotation is performed against a resistance presented due to the fact that a protrusion 30 on the outer wall of the ampoule holder rests in one of a number of depressions 31 circumferentially provided in the inner wall of said first division of the housing as shown in the cross-sectional view in FIG. 3. The angular spacing of the depressions are appropriately made so that a dose of one unit is set when the protrusion is moved from one depression to the neighbouring depression so that the number of clicks heard and felt during the dose setting rotation corresponds to the size of the set dose.

The rotation of the ampoule holder is due to the friction in the engaging threads 5 and 7 transmitted to the piston rod 6 and further through the unidirectional coupling to the piston rod guide 14 although the torque is transmitted in a such a direction that the pawl will intend to click over the pawl wheel teeth 10. However, before this click function is performed a reluctance have to be overcome. This reluctance is obtained by providing the pawl 13 with a protrusion 29 at its end engaging the pawl wheel teeth 10 and by providing depressions 32 in the ramp shaped edges 12 of the pawl wheel teeth into which depressions the protrusion 29 on the pawl 13 will rest. Before the clicking release of the coupling is obtained a torque sufficient to lift up the protrusion 29 of the pawl 13 from the depression 32 in the ramp shaped edge 12 must be provided. Altogether a moderate torque can be transmitted from the rotated ampoule holder 2 to the driver tube 26. As the hooks 28 at the proximal end of the driver

tube 26 engage the slots 22 in the dose scale drum extension 21 the dose scale drum will be rotated and be screwed upwards in the second division of the housing 1 and the injection button 23 will be lifted to protrude from the proximal end of the housing 1. As only a small torque is needed to screw up the dose scale drum this is obtained without releasing the unidirectional coupling to its clicking release function mode. The size of the set dose can currently be seen on the part of the dose scale drum which is presented in the window 18. If a too large dose has been set the ampoule holder can be rotated in a clockwise direction until the number corresponding to the size of the wanted doe is presented in the window 18.

To inject the set dose the injection button 23 is pressed home into the housing 1. Thereby the dose scale drum 17 is pressed in the distal direction and due to the thread connection between said drum and the housing 1 a torque is exerted on the drum rotating this drum in a clockwise direction. Said torque is via the slots 22 in the drum extension 21 and the hooks 28 at the end of the driver tube 26 and this tube itself transmitted to the piston rod guide 14. The pawls 13 on the piston rod guide are allowed to rotate in the clockwise direction when the torque is strong enough to overcome the reluctance provided by the protrusions 29 on the pawls engaging the depressions 32 in the ramp shaped edges of the pawl wheel teeth.

Such a strong torque is provided if only the inject button 23 is pressed hard enough. The piston rod guide 14 will now rotate clockwise with the unidirectional coupling working in its clicking released mode and the piston rod will be rotated clockwise too and will thereby be screwed through the wall 4 further into the ampoule accommodating compartment 8. The unidirectional coupling will never allow an anticlockwise rotation of the piston rod guide and the piston and this way it is ensured that the pressure foot 9 will never be drawn out of abutment with the piston in a not shown ampoule in the compartment 8.

In the shown embodiment the end wall 4 with its threaded bore forms a nut member relative to which the piston rod is rotated by the piston rod guide 14 and the driver tube 26. Embodiments may be imagined wherein the piston rod guide is provided in the wall 4 and a nut element is rotated by the driver tube and such embodiment will not be beyond the scope of the invention.

Another embodiment is described with reference to the FIGS. 6–10. Elements corresponding to elements in the embodiment described with references to the FIGS 1–5 are provided with the same reference numbers. Different from the embodiment in FIGS. 1–5 is the fact that the injection button 23 and not the dose scale drum 17 is provided with an extension 33, and that the driver tube 26 is omitted. Further the injection button 23 is provided with a flange 32 which abuts the end of the housing when the injection button is pressed home. The extension 33 serves as a journal for the dose scale drum 17 which is free to rotate on this journal but bound to follow axial movements of the injection button 23 due to hooks 34 at the end of the extension 33. A longitudinal bore 35 in the injection button and its extension 33 is provided with an internal helical rib 36 engaging a corresponding helical groove in an enlargement 37 at the proximal end of the piston rod to form a thread connection between said button 23 and said piston rod 6. The pitch of this thread connection is so that a not self locking thread connection is formed.

To set a dose the injection button 23 is manually rotated in a clockwise direction. Thereby this button is screwed outwards from the housing 1 as the piston rod 6 will through the piston rod guide 14 and the unidirectional coupling be kept inrotatable although said unidirectional coupling in influenced by a torque in its release direction, however, due to the provided initial reluctance the piston rod guide 14 will not immediately be rotatable. In its movement outwards the injection button 23 will draw the dose scale drum 17 with it. When this drum is moved axially in the housing it will be rotated due to the not self locking thread connection between said drum 17 and the housing 1.

By this construction the thread along which the injection button is screwed outwards and the tread along which the dose scale drum is rotated in the housing may be different.

A click connection corresponding to the one established between the cartridge holder 2 and the housing 1 in the embodiment according to FIG. 1 is in the embodiment according to FIG. 6 appropriately provided between the injection button 23 and the housing 1 where one or more protrusions 38 provided on the inner wall of the housing engages grooves 39 in a cylindrical outer wall of the button 23. Thereby axial movement of the injection button is allowed in all its possible angular positions.

When the injection button is pressed to inject a set dose said button will be maintained inrotatable during its axial movement as the locking between the above mentioned protrusions on the inner wall of the housing and grooves on the outer wall of the button is strong enough to absorb the torque exerted on the injection button when it drives the piston rod to rotation in a clockwise direction after having overcome the reluctance against rotation in the release direction of the unidirectional coupling.

The embodiment shown in FIGS. 11, 12 and 13 has the housing 1 with the window 18. The end wall 4 with the internal thread 5 is provided in a separate member 40 which is mounted in an end of the housing, the member 40 having protrusions 41 engaging slots 42 in the housing to lock the member 40 to the housing 1. Further the member 40 has at its periphery longitudinal recesses 43 which are engaged by not shown internal ribs in the housing to lock the member 40 against rotation relative to the housing 1. Further protrusions 44 on the ampoule holder 2 engage the slots 42 to lock the ampoule holder 2 to the housing 1.

The piston rod 6 engages by its external thread 7 the internal thread of the end wall 4 and is at its end in the ampoule holder terminated by a pressure foot 9 relative to which the piston rod 6 is rotatable. A driver tube 45 is at one end provided with the pawl 13 which engages pawl wheel teeth in the member 40 and is held between a ring shaped wall 46 in the housing and the end wall 4 in the member 40 to keep the driver tube 45 from axial movement but allowing it to rotate. On its inner wall the driver tube 45 has a key engaging a longitudinal recess in the piston rod 6. Thereby rotation of the driver tube is transmitted to the piston rod 6 whereas the piston rod can move freely in the axial direction of the driver tube 45. On its outer wall the driver tube 45 has an outer thread 47 which engages an inner thread 50 in a nut member 48 which has at its distal end a flange 49 and is at its proximal end provided with a part 51 with reduced diameter to which part one end of a tubular part 52 which at its other end carries a button 23 is secured.

In the proximal end of the housing 1 a bushing 53 is secured to be non rotatable an non displaceable relative to said housing 1 the rotational locking being obtained by lugs 54 at the proximal end of the housing engaging recesses 55 at the periphery of the bushing 53. A guide member 56 is longitudinally displaceable in the bushing 53 but inrotatable relative to said bushing and consequently relative to the housing 1. The guide member has at its distal end an annular

end wall 57. The part 51 of the nut member 48 is passed through the opening of said end wall 57 and has a bead 58 gripping into a circumferential inner recess in the wall of annular opening through said end wall to keep the bushing 53 secured to said part 51 so that this part can be rotated but not axially displaced in relation to the bushing 53. The scale drum 17 is journalled on the nut member 48 and is held on this nut member by having a flange 90 held between the end wall 57 of the guide member 56 and the shoulder formed where the part 51 connects to the nut member 48.

The button 23 is held rotatably on the guide member 56 which has a ring bead 59 engaging a circumferential recess 60 in the inner wall of the button 23 which recess 60 is somewhat broader than than the bead 59 so that the button in excess of being rotatable on said bushing 53 can be axially displaced a distance defined by the width of the recess 60 relative to the width of the bead 59. The button 23 is coupled to the nut member 48 by internal ribs 61 in the tubular part 52 engaging slots 62 in the proximal part of the part 51 of the nut member 48. This coupling forces the button 23 and the nut member 48 to follow each other in rotational movements but allow a minor relative axial displacement.

The proximal end surface of the guide member 56 has one or more axially directed protrusions 63 which can co-operate with radial recesses 64 in the bottom of the button 23, but mainly a biasing keeps these recesses and protrusions out of engagement. Further the guide member has at its proximal end at least one radial protrusion 65 which is biased to engage axial recesses 66 in an inner wall of the button to produced a click sound each time the button is rotated relative to the bushing so that the protrusion jump from one recess to the neighbour recess.

To set a dose the button 23 is rotated in a clockwise direction. This rotation is due to the coupling between the ribs 61 and the slots 62 transmitted to the nut member 48 which is then screwed in distal direction along the driver tube 45 which is held inrotatably in the housing due to the reluctans of the pawl 13 to move along the pawl teeth in the member 40. The movement of the nut member 48 in proximal direction makes the scale drum 17, the guide member 56, and the tubular part 52 with the button move in proximal direction so that the button is elevated over the end proximal end of the housing 1. A to high set dose can be reduced by rotating the button in an anti clockwise direction.

During the rotation of the button the radial protrusion 65 of the guide member 56 clicks from one axial recess 66 to the other. The distance between can appropriately be chosen so that a click corresponds to a changing of the set dose by one international unit up or down. Due to engagement between the helical grove on the cylinder wall of the scale drum and a helical rib on the inner wall of the housing the movement of the dose scale drum 17 will rotate and displace said drum so that the set dose is shown in the window 18.

When the dose scale drum is displaced outwardly in the housing a steep front side of a saw tooth 91 at the proximal end of the dose scale drum 18 will abut a steep front side of a similar tooth 92 on the bushing whereby the rotation of the dose scale drum is stopped to indicate that a maximum dose has been set.

To inject the set dose the button 23 is pressed. Thereby the bias keeping the protrusions 63 and the recesses 64 out of engagement is overcome and the said engagement is established. The button 23 is now locked relative to the guide element 56 which is again locked against rotation relative to the bushing 53 and consequently relative to the housing 1. The coupling between the tubular part 52 and the nut member 48 makes this nut member inrotatable relative to the housing so an axial movement of said nut member in a distal direction will due to the not self locking thread coupling between this nut element and the driver tube 45 make this driver tube 45 rotate in a clockwise direction and due to the key/groove coupling between the driver tube 45 and the piston rod 6 said piston rod will be screwed through the end wall 4 further into the ampoule holder compartment. The locking of the button 23 against rotation during the injection ensures that the set dose is not inadvertently changed during the injection.

In the embodiment shown in FIG. 14 separate buttons are provided for the dose setting and the injection. Corresponding to previously described embodiments this one has a housing 1 and a driver tube 67 which is rotatable in only one direction due to a pawl which engage pawl wheel teeth in a part secured in the distal end of the housing. Trapping of the pawl between the member 40 and a ring shaped wall 46 in the housing fixes the driver tube against axial movement. On the outer wall of the driver tube 67 an axial rib 68 is provided which rib engages an axial recess 69 in a tubular injection element 70 to transmit rotation of said injection element to the driver tube 67.

At the proximal end of the housing 1 a dose setting button 71 is mounted so that this button can be rotated but not axially displaced relative to the housing 1. This is obtained by the fact that the dose setting button 71 on a part fitting into the housing has a ring shaped bead 72 which engages a mating circumferential recess 73 in the inner wall of the housing. Outside the housing the dose setting button has a part having a diameter corresponding to or being larger than the diameter of said housing which part can be provided with axial ribs 74 to ensure a good grip by the setting of a dose. The dose setting button 71 has a central bore the inner wall of which has a helical recess 75 engaging a helical rib 76 provided on the outer wall of the proximal part of the injection element 70 which element passes through the bore of the dose setting button 71. The outer wall of the distal part of the injection element 70 forms a journal for the scale drum 17 which through an outer helical recess engaged by an internal helical rib 16 in the housing is rotated to show the set dose in the window 18 when the scale drum is displaced axially in the housing. The proximal end of the injection member is terminated by an end wall 77 which carries an injection button 78 which is by a pivot pin 79 journaled in a central bore in said end wall 77.

To set a dose the dose setting button 71 is rotated in a clockwise direction. As the injection member is kept non rotatable by its coupling to the driver tube 67 the collaboration between the helical recess 75 in the inner wall of the dose setting button 71 and the helical rib 76 on the outer wall of the injection element 70 will screw the injection element out through the dose setting button so that the injection button 78 is lifted up from the proximal end of the housing. Although the driver tube 67 with its pawl can be rotated in the clockwise direction an initial torque is needed which is larger than the torque transmitted from the dose setting button to the injection element.

To inject a set dose the injection button 78 is pressed and the injection element is moved back into the housing. The co-operation of the helical recess 75 in the inner wall of the dose setting button 71 and the helical rib 76 on the outer wall of the injection element 70 will now make the injection element rotate in a clockwise direction and if only the injection button is pressed hard enough a torque is produced large enough to overcome the initial reluctance of the pawl mechanism against rotation in said clockwise direction.

The separation of the dose setting button 71 and the injection button 78 makes it less likely that the dose setting button is inadvertently operated during the injection.

FIGS. 15, 16 and 17 illustrates still another embodiment. To maintain a clockwise rotation of a dose setting button for increasing the set dose the pawl mechanism working between the driver tube and the housing is turned so that it bars clockwise rotation and reluctantly allows anticlockwise rotation of the driver tube. Further the thread of the piston rod and the thread in the end wall of the housing is so designed that an anticlockwise rotation of the piston will screw the piston rod through said end wall and into the cartridge holder compartment. The piston rod has a not round cross-section and fits through the driver tube bore which has a corresponding not round cross-section. This way rotation is transmitted whereas the piston rod is allowed to move longitudinally through the driver tube.

A scale drum **80** is in its outer wall provided with a helical track which is engaged by a helical rib **16** along the inner wall of the housing **1**. At its proximal end the scale drum **80** has a diameter exceeding the inner diameter of the housing to form a dose setting button **81** which on its cylindrical outer wall is knurled to ensure a good finger grip.

A bushing **82** having a flange **83** at its proximal end and having a pair of opposite longitudinal slots **84** through its side walls fits into the scale drum **80** and over the driver tube **85** which tube has on its outer wall hooks **86** engaging the slots **84** of the bushing **82** whereby the bushing **82** and the driver tube **85** is coupled to each other so that rotation but not longitudinal displacement is transmitted between said two elements.

In the dose setting button a compartment is provided having a cylindrical side wall circumferentially provided with longitudinal recesses and a bottom with a rosette of teeth having a triangular cross-section. The flange **83** of the bushing **82** is adopted in said compartment and has at its periphery a radial protrusion **87** which is biased toward the side wall of the compartment. At its distal side the flange **83** has a rosette **93** of teeth which can be brought into engagement with the rosette at the bottom of the compartment.

The bushing **82** is mounted in the scale drum **80** with protrusion on the outer wall of the bushing **82** engaging recesses in the inner wall of the scale drum **80** so that a limited movement of the bushing in the scale drum is allowed so that the bushing can be moved axially relative to the scale drum to make or not make the teeth of said rosettes engage each other. An injection button **88** is rotatably mounted with a pivot pin **94** journaled in an end wall of the bushing **82**.

When a dose is set by rotating the dose setting button **81** in a clockwise direction, the scale drum is screwed out of the housing and the dose setting button is lifted away from the proximal end of the housing. The bushing is kept non rotated due to its coupling to the driver tube which is locked against clockwise rotation and if a set dose is reduced by rotating the dose setting button **81** in an anticlockwise direction the pawl mechanism working between the driver tube and the housing is sufficient reluctant to rotate in its not blocking direction to prevent the bushing **82** from following this anticlockwise rotation. Therefore by the rotation of the dose setting button **81** in any direction the radial protrusion **87** on the flange **83** of the bushing **82** will click from one of the axial recess in the inner wall of the dose setting button **81** to the next one, the recesses being so spaced that one click corresponds to a chosen change of the set dose, e. g. one unit or a half unit. During the setting the rosette in the dose setting button forces the rosette **93** on the flange **83** of the bushing **82** out of engagement.

When the injection button **88** is pressed to inject the set dose the said rosettes are pressed into engagement so that the bushing **82** will follow the anticlockwise rotation of the dose setting button **81** which is induced by the thread engagement between the helical track of the scale drum **80** and the rib **16** in the housing when the scale drum **80** is pressed back into said housing. The bushing will rotate the driver tube **85** in an anticlockwise direction which the pawl mechanism reluctantly allows an the piston rod is thereby screwed further into an ampoule **89** in the ampoule holder **2**.

By this device the risk for inadvertent operation of the dose setting button **81** during the injection is eliminated. Further the device consist of a minimum of parts whereby the manufacturing is made easy.

We claim:

1. An injection syringe for apportioning set doses of a medicine from a cartridge containing an amount of medicine sufficient for the preparation of a number of therapeutic doses, comprising

a housing;

a piston rod having a not circular cross-section and an outer thread

a piston rod drive comprising two elements

a) a piston rod guide mating the not circular cross-section of the piston rod to allow axially displacement but not rotatation of the piston rod in relation to said piston rod guide, and

b) a nut member which is not axially displaceable in the housing and which has an inner thread mating the thread of the piston rod to form a self locking thread connection,

a dose setting mechanism comprising a not self locking thread connection along which an injection button by rotation of a dose setting element relative to said housing is screwed out from the proximal end of the housing to project from this proximal end a distance determined by the angle of said rotation and which thread connection by axial returning of the injection button transforms this axial movement to a rotation of one of the piston drive elements relative to the other, characterised in that a unidirectional coupling is provided between the nut member and the piston rod guide allowing rotation of these parts relative to each other in one direction but not in the opposite direction, the allowed rotation being one by which the piston rod is transported in a distal direction in the syringe, the coupling being so designed that an initial reluctance set large enough to resist a torque exerted on the coupling by the dose setting has to be overcome before rotation takes place.

2. An injection syringe according to claim **1**, characterised in that a click coupling providing an moderate resistance against rotation in either directions is established between the housing and the element rotated relative to this housing to set a dose.

3. An injection syringe according to claim **1**, characterised in that the unidirectional coupling comprises a pawl sliding over a pawl wheel with teeth having a steep front edge and a ramp shaped trailing edge.

4. An injection syringe according to claim **3**, characterised in that the trailing edges of the pawl wheel teeth has a depression engaged by a mating protrusion on the pawl.

5. An injection syringe according to claim **1**, characterised in that a dose scale drum has in its surface a helical track engaged by a helical rib on the inner side of the housing to form a not self locking thread connection between the housing, and that the dose scale drum and is coupled to the injection button to be moved axially with this button.

6. An injection syringe according to claim **5**, characterised in that the thread connection by which the injection button is lifted by setting a dose is the thread connection between the dose scale drum and the housing.

7. An injection syringe according to claim 1, characterised in that the element rotated relative to the housing is the injection button and that the not self locking thread connection which determines the lifting of the injection button is an inner thread in a bore in the injection button engaging an outer thread on a part with enlarged diameter of the piston rod.

8. An injection syringe according to claim 1, characterised in that the piston rod guide is mounted in a driver tube in which tube the piston rod is axially displaceable but is rotated with said tube, and that the not self locking thread connection which determines the lifting of the injection button is provided between the driver tube and a part which is axially displaceable with the injection button

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,004,297
DATED : December 21, 1999
INVENTOR(S) : Steenfeldt-Jensen et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 12,
Line 23, please delete "rotation", and insert -- rotation --.

Signed and Sealed this

Twenty-seventh Day of November, 2001

Attest:

Nicholas P. Godici

Attesting Officer

NICHOLAS P. GODICI
Acting Director of the United States Patent and Trademark Office

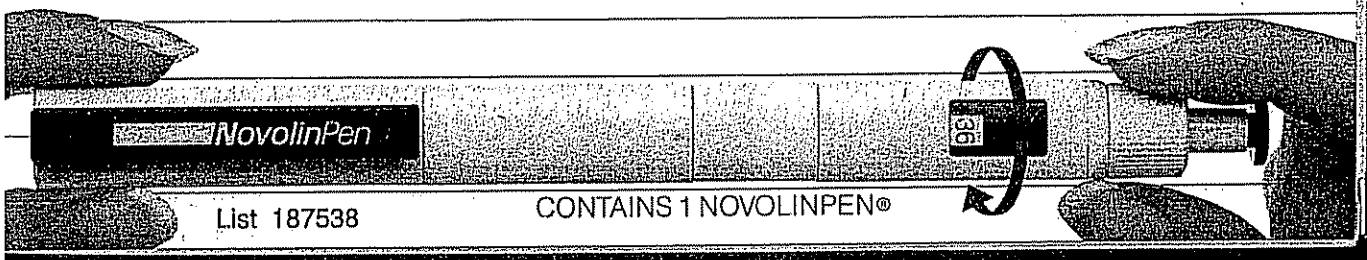
EXHIBIT 21

NovolinPen® *Novo Nordisk™*

Dial•A•Dose
Insulin Delivery Device

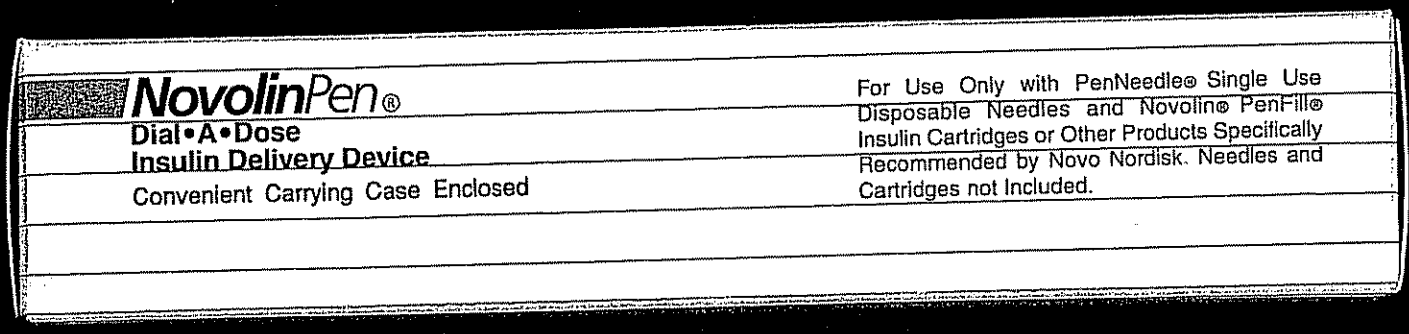
- Portable
- Accurate
- Easy-to-Use

- 2 to 36 Unit Dial-A-Dose



List 187538

CONTAINS 1 NOVOLINPEN®

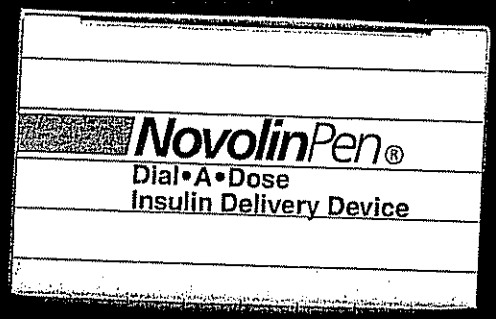

NovolinPen®
Dial•A•Dose
Insulin Delivery Device
Convenient Carrying Case Enclosed
For Use Only with PenNeedle® Single Use Disposable Needles and Novolin® PenFill® Insulin Cartridges or Other Products Specifically Recommended by Novo Nordisk. Needles and Cartridges not Included.

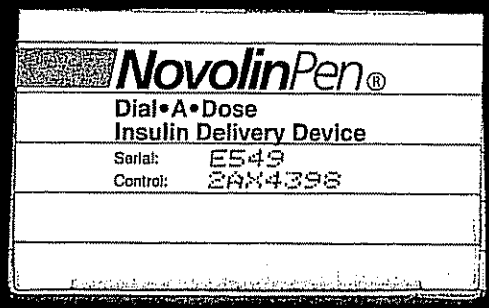
List 187538

NovolinPen®, PenFill®, Novolin®
and PenNeedle®, are registered
trademarks of Novo Nordisk A/S

For information contact:
Novo Nordisk Pharmaceuticals Inc.
Princeton, NJ 08540

Manufactured in Denmark for
Novo Nordisk A/S
DK 2880 Bagsvaerd, Denmark


NovolinPen®
Dial•A•Dose
Insulin Delivery Device


NovolinPen®
Dial•A•Dose
Insulin Delivery Device
Serial: E549
Control: 2AM4398

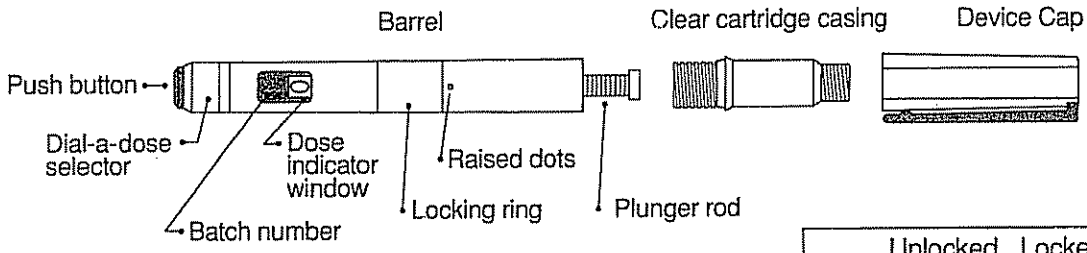
NovolinPen®

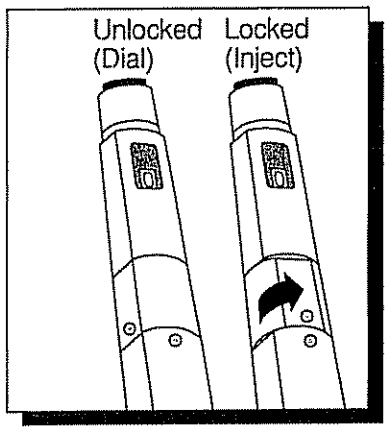
Dial-A-Dose
Insulin Delivery Device

Instructions For Use

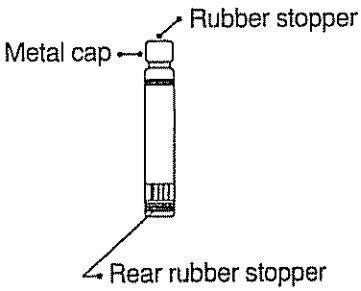
Open this flap
for a
drawing of the
NovolinPen®

NovolinPen®

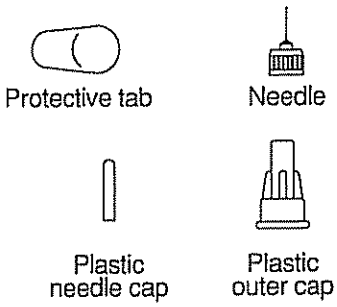




Novolin®PenFill® Cartridge



PenNeedle® disposable needle



Need Help? Call 1-800-727-6500

Welcome to Your NovolinPen® Dial-a-Dose Insulin Delivery System

Before you use the NovolinPen®, read this booklet carefully so that you understand how to assemble, operate, and take care of it.

Introduction

You have just received the NovolinPen insulin delivery device.
To use the NovolinPen, you will need:

- Novolin® PenFill® insulin cartridges.
- PenNeedle® single-use disposable needles.
- Alcohol swabs.

The NovolinPen offers you a convenient way to deliver an accurate dose of 2 to 36 units of insulin in 2-unit increments (2, 4, 6, 8, and so on, up to 36). Handle your NovolinPen as you would any precision instrument. Follow the instructions for use, storage, and cleaning, and keep this booklet handy for future reference. If you need further assistance, call 1-800-727-6500.

How to Use This Booklet

This booklet gives you step-by-step instructions for using the NovolinPen.

Begin by reviewing the drawing of the parts of the NovolinPen, PenFill cartridge, and PenNeedle. The page opens out so that you have a handy reference while you read the rest of the booklet.

Each page contains a drawing in the upper left, with numbered instructions to the right of the drawing. **Important additional information is given below the drawing.**

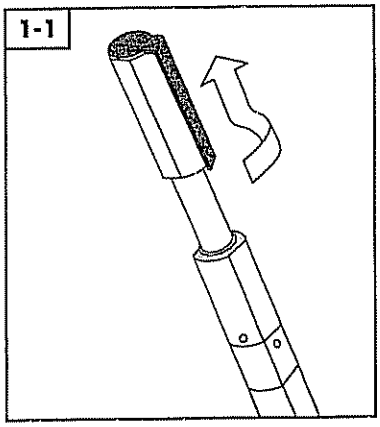
We suggest that you **read the text and look at the drawings** to make sure you understand each step thoroughly.

Important Things to Know

- **The NovolinPen is not recommended for the blind or visually impaired without the assistance of a sighted individual trained to use it.**
- If you use two types of insulin, always check that the PenFill cartridge in your NovolinPen contains the correct type of insulin. Novo Nordisk suggests you use a different NovolinPen for each type.
- **Always keep a spare NovolinPen (or insulin syringe) available in case your NovolinPen is lost or damaged.**
- **Keep the NovolinPen out of the reach of children.**
- **The NovolinPen is not recommended for pediatric use.**
- Keep the NovolinPen away from extreme heat. Extreme heat will not only damage the insulin, but it may also damage the device.
- **The NovolinPen should only be used with Novolin PenFill insulin cartridges, PenNeedle single-use disposable needles, or other products specifically recommended by Novo Nordisk.** Novo Nordisk is not responsible for any consequences arising from the use of the NovolinPen with products that are not recommended by Novo Nordisk.
- See Important Notes on pages 27-29.

Table of Contents

1-1



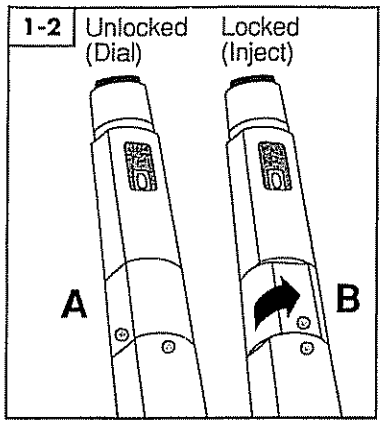
Section 1 — Preparing the NovolinPen

Remove the device cap:

1. Remove the NovolinPen from the case.
2. Gently twist the device cap until the cap separates from the barrel.
3. Pull the device cap straight up to remove it.

The device cap must be taken off and put back on in the proper position.

Need Help? Call 1-800-727-6500



Check the position of the locking ring:

4 Hold the NovolinPen with the blue pushbutton pointing upward.

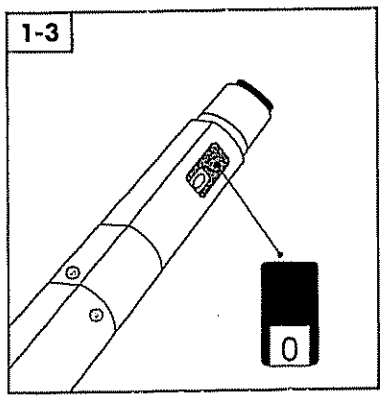
5 Be sure the locking ring is in the **unlocked** position (Position **A**: raised dots are **not** lined up).

- If it is in the locked position (Position **B**: dots are lined up), twist it until it is in the **unlocked** position.

The position of the locking ring determines whether or not insulin can be injected. In the:

- **Unlocked position (A)** — The raised dots are **not** lined up and insulin cannot be injected.
- **Locked position (B)** — The raised dots **are** lined up and insulin can be injected. It is called the "locked" position because it "locks in" the dose you select.

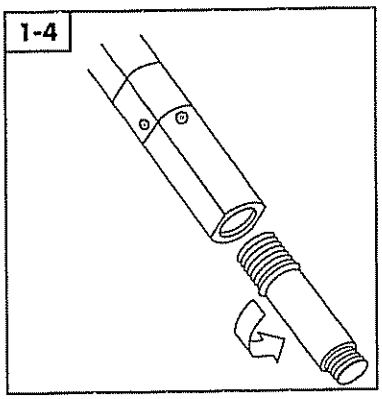
The locking ring must be in the unlocked position (A) when you insert the PenFill cartridge, attach the PenNeedle, and dial a dose. So, **keep the locking ring in the unlocked position until you are ready to do an air shot or give an injection.**



Check the dose setting:

6 Be sure the dose indicator window shows zero (0).

If needed, turn the dial-a-dose selector until zero (0) appears in the window and you feel resistance.

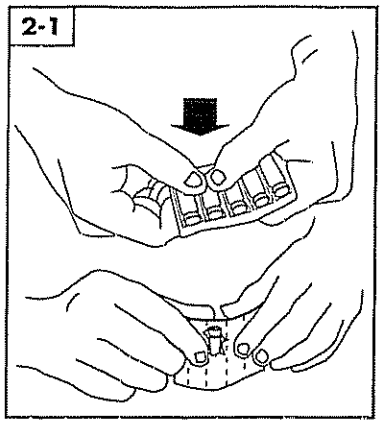


Separate the clear cartridge casing from the barrel:

7 Unscrew and remove the clear cartridge casing from the barrel.

Need Help? Call 1-800-727-6500

2-1



Section 2 — Inserting the Novolin PenFill Cartridge

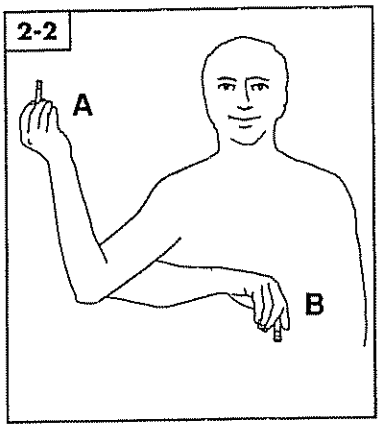
1 To remove the PenFill cartridge from its wrapper, push the cartridge through the foil side of the packaging.

Each PenFill cartridge contains a total of 150 units of insulin. There are five cartridges to a box. If you need more than one type of insulin, make sure you are using the correct type.

Each PenFill cartridge is for single-person use only. DO NOT use the same cartridge for more than one person, even though you attach a new PenNeedle for each injection. This will prevent the spread of disease.

Never try to refill a used PenFill cartridge.

2-2



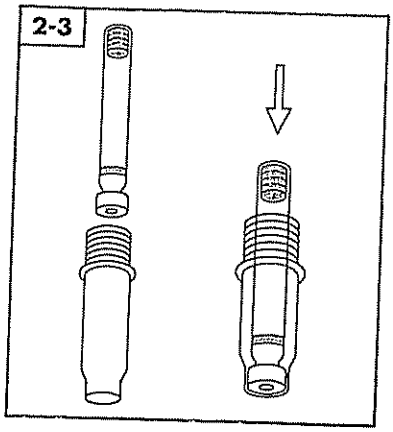
If you use Novolin® 70/30 or Novolin® N insulin, mix the insulin:

2 Turn the PenFill cartridge up and down between positions A and B, as shown.

3 Repeat this mixing step at least 10 times or until the insulin looks uniformly white and cloudy.

Need Help? Call 1-800-727-6500

2-3



Insert the cartridge:

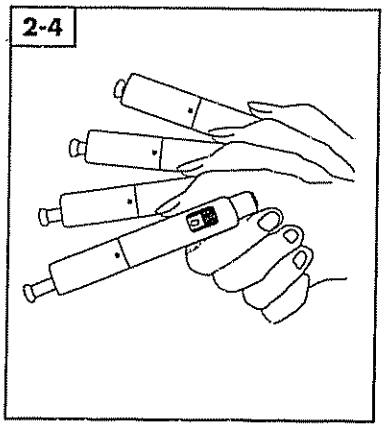
4 Hold the clear cartridge casing so the wider opening is up.

5 Insert the PenFill cartridge into the top of the casing, metal cap first.

6 Push the cartridge as far as it will go, until it fits snugly in the bottom of the casing.

The metal cap of the PenFill cartridge surrounds the end of the cartridge, like the cap on a bottle. In the center is the front rubber stopper.
The rear rubber stopper is inside the bottom of the cartridge and has an X on it.

2-4



Extend the plunger rod:

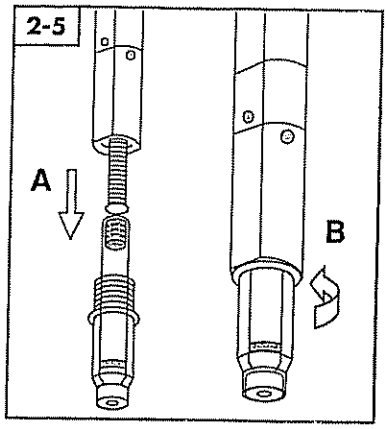
7 Hold the barrel of the NovolinPen at the end, near the dose indicator window.

8 Snap your wrist downward quickly, as if you were shaking down a thermometer, until the plunger rod sticks out completely from the barrel.

9 **Gently** pull the plunger rod to make sure it is fully extended.

To make certain you receive the correct dose, the plunger rod must be fully extended before you insert it into the PenFill cartridge.

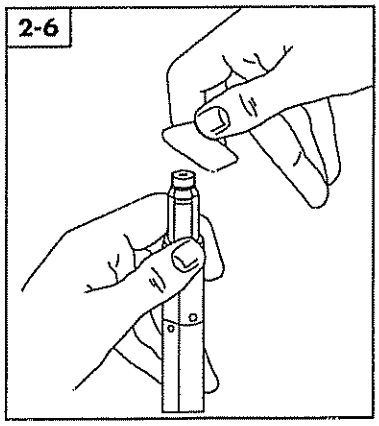
Need Help? Call 1-800-727-6500



Re-attach the clear cartridge casing:

10 Insert the plunger rod into the PenFill cartridge so that it rests on the rear rubber stopper (**A**).

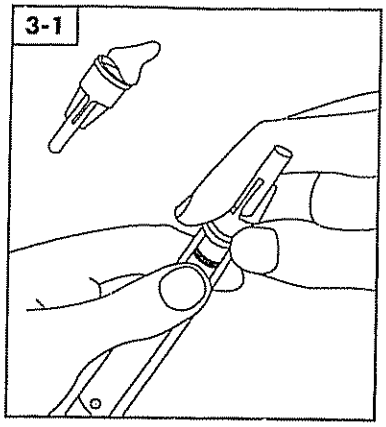
11 Holding the NovolinPen in the same position, screw the clear cartridge casing **up** into the barrel securely (**B**).



12 Wipe the front rubber stopper at the exposed end of the clear cartridge casing with an alcohol swab.

You must wipe the front rubber stopper with an alcohol swab before each injection, even if you are using the same cartridge.

Need Help? Call 1-800-727-6500



Section 3 — Attaching the PenNeedle

1. Remove the protective tab from the PenNeedle.
2. With gentle pressure, screw the PenNeedle completely onto the clear cartridge casing.

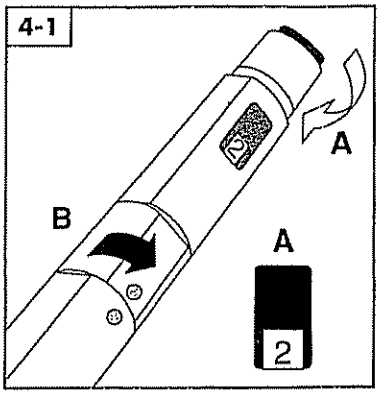
Section 4 — Doing the Air Shot

Small amounts of air may collect in the PenNeedle and PenFill cartridge during normal use. To prevent the injection of air and make certain insulin is delivered, **you must do an air shot before each injection.**

- Before starting the air shot procedure, the locking ring must be in the **unlocked position and the dose indicator window must show zero** (0).

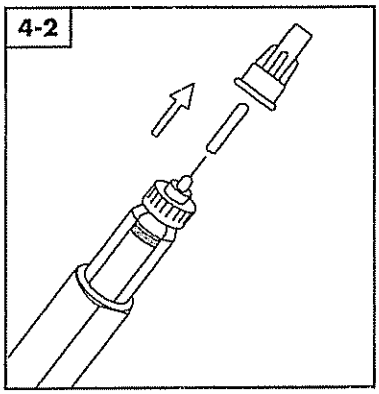
If you use Novolin 70/30 or Novolin N insulin and have used the cartridge for previous injections, make sure there are at least 12 units left in the cartridge before you start. This is necessary to properly mix the insulin.

- Try to dial the dial-a-dose selector to 12. **The number in the dose indicator window will not show more units than are available, even if you force the selector to turn.**
- If the indicator shows less than 12, insert a new cartridge. (See Section 7 for instructions on removing a cartridge and Section 2 for inserting a new one.)
- Turn the dial-a-dose selector until zero appears in the dose indicator window.



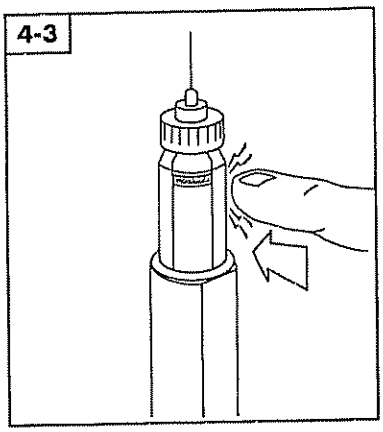
Set the NovolinPen for the air shot:

1. Turn the dial-a-dose selector until 2 appears in the dose indicator window (A).
2. Twist the locking ring 1/4 turn into the locked position. The dots will line up with each other (B). *Insulin can only be delivered if the locking ring is in the locked position.*



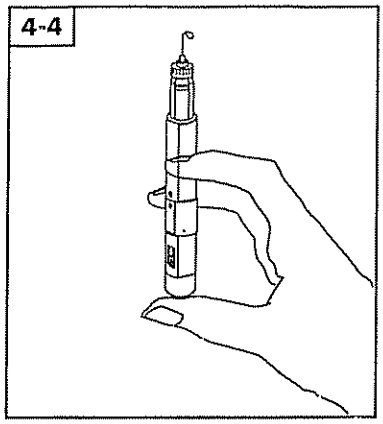
Uncap the needle:

3. Pull off the plastic outer cap and set it aside.
4. Pull off the inner needle cap and discard.



Do the air shot:

5. Hold the NovolinPen with the needle pointing upward.
6. Tap the clear cartridge casing with your finger a few times to raise any air bubbles that may be present to the top of the cartridge.



7 Press the blue pushbutton at the dial-a-dose selector end of the NovolinPen as far as it will go. A drop of insulin should appear at the needle tip.

If no insulin appears, repeat the steps as follows:

a. Return the locking ring to the unlocked position.

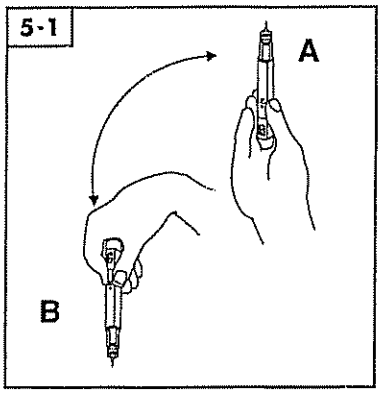
b. Turn the dial-a-dose selector until zero (0) appears in the window **and you feel resistance.**

c. Dial 2 units.

d. Twist the locking ring into the **locked** position.

e. Tap the clear cartridge casing with your finger.

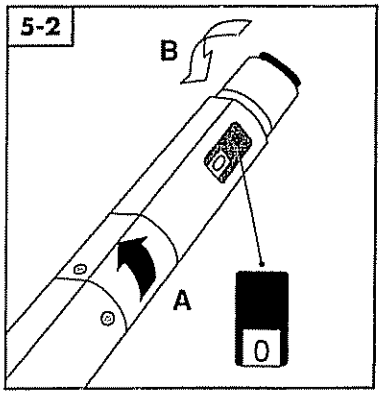
f. Press the blue pushbutton.



Section 5 — Giving the Injection

For users of Novolin 70/30 or Novolin N insulin: Always remix the insulin.

1 To remix the insulin, turn the NovolinPen up and down between positions **A** and **B** 10 times.



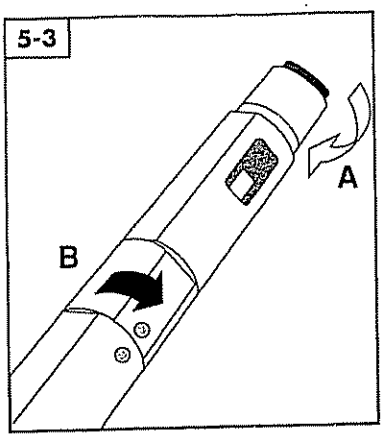
Reset the NovolinPen:

2 Return the locking ring to the **unlocked** position (**A**).

3 Turn the dial-a-dose selector until zero (0) appears in the dose indicator window **and you feel resistance** (**B**). *This resets the device after the air shot.*

Need Help? Call 1-800-727-6500

5-3



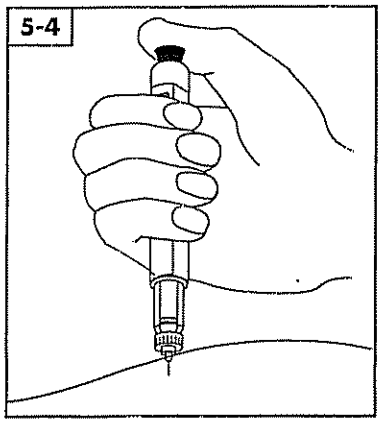
Select the dose:

4 Turn the dial-a-dose selector until you see the correct number of units in the dose indicator window (**A**). **Do not use the clicking sound as a guide for selecting your dose.**

5 Twist the locking ring 1/4 turn into the **locked** position. The dots will line up with each other (**B**). *The insulin can only be injected if the locking ring is in the locked position.*

The NovolinPen can deliver from 2 to 36 units of insulin in 2-unit increments (2, 4, 6, 8, and so on, up to 36).
Steps 4 and 5 tell you how to select a dose. The dial-a-dose selector should not be turned when the locking ring is in the locked position. If you select the wrong dose, repeat steps 2 and 3 on the preceding page.

5-4

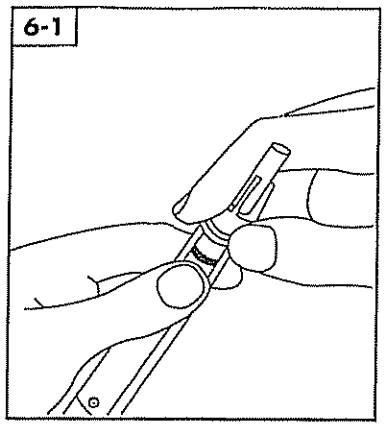


Give the injection:

6 Insert the needle in the correct site on the body. (Use the injection technique recommended by your doctor.)

7 Press the pushbutton **as far as it will go** to deliver the insulin.

If the locking ring is in the **unlocked** position, no insulin will be delivered.



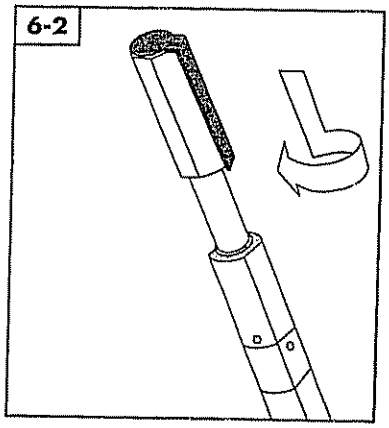
Section 6 — Removing the PenNeedle

Remove the needle:

1. After the injection, return the locking ring to the **unlocked** position.
2. Turn the dial-a-dose selector until zero (0) appears in the dose indicator window.
3. Replace the plastic outer cap.
4. Hold the clear cartridge casing firmly while you unscrew the PenNeedle.
5. Place the used PenNeedle in a puncture-resistant disposal container.

The PenNeedle must be removed immediately after each injection. If the needle is not removed, some liquid may leak out of the PenFill cartridge. This causes a change in the strength of Novolin 70/30 and Novolin N insulin.

For information on how to properly dispose of needle containers, call your local trash disposal authorities.



Replace the device cap:

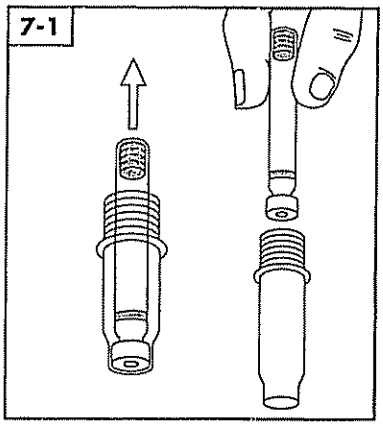
6. Hold the barrel of the NovolinPen.
7. **Very gently** place the device cap on the clear cartridge casing.
8. Turn the device cap to the left, until it clicks into place.

Need Help? Call 1-800-727-6500

Section 7 — Removing the PenFill Cartridge

You will need to remove the cartridge for the following reasons:

- **If you use Novolin® R insulin:** When the cartridge is empty.
- **If you use Novolin 70/30 or Novolin N insulin:** When you have less than 12 units left in the cartridge.
- **If you use two types of insulin:** To change to the correct type.



Remove the cartridge:

1. Remove the device cap.
2. Unscrew the clear cartridge casing from the barrel.
3. Hold the clear cartridge casing with one hand.
4. Grasp the exposed end of the cartridge with the thumb and index finger of the other hand.
5. Pull the cartridge out of the clear cartridge casing.

Function Check

You should check the functioning of your NovolinPen once a month or before starting a new box of PenFill cartridges. The Function Check is done by delivering 20 units of insulin into the plastic outer cap. You will not be injecting insulin into your body.

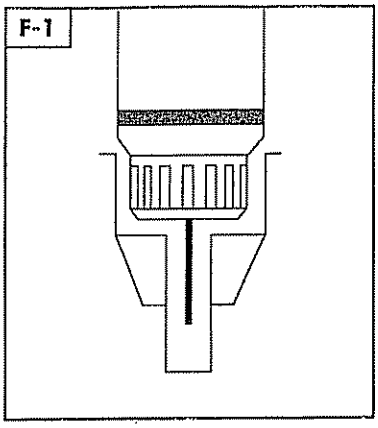
Always check the functioning of the NovolinPen if you suspect it has been damaged or if you are uncertain that it is delivering the correct dose.

To perform the function check:

1. Turn the dial-a-dose selector until 20 appears in the dose indicator window to make sure there are at least 20 units of insulin in the PenFill cartridge. If there are fewer, remove the old cartridge (p. 20) and insert a new cartridge (pp. 4–9).
2. Attach a PenNeedle (p. 10).
3. Do an air shot (pp. 11–14).
4. Return the locking ring to the unlocked position.
5. Turn the dial-a-dose selector until zero (0) appears in the dose indicator window **and you feel resistance.**

Need Help? Call 1-800-727-6500

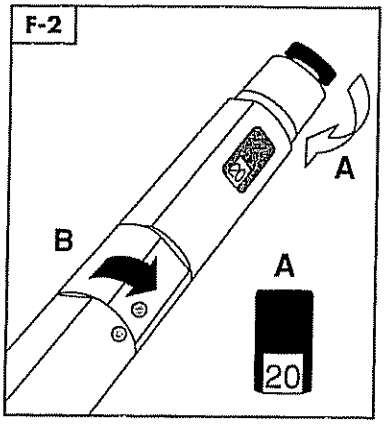
F-1



6 Place the plastic outer cap over the exposed needle. *Do not replace the inner needle cap.*

The bottom part of the plastic outer cap holds 20 units of insulin.

F-2



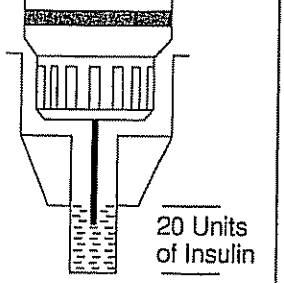
Deliver 20 units into the plastic outer cap.

7 Turn the dial-a-dose selector so the dose indicator window shows 20 (**A**).

8 Twist the locking ring 1/4 turn to the **locked** position. *The dots will line up with each other* (**B**).

Need Help? Call 1-800-727-6500

F-3



9 Hold the NovolinPen so that the PenNeedle is pointing downward.

10 Press the pushbutton **as far as it will go.**

The insulin should fill the bottom part of the plastic outer cap. This indicates the device is functioning properly.

If the insulin **does not fill or overfills** this part of the cap, repeat the function check with a new PenNeedle and plastic outer cap.

If the second function check also shows under- or overfilling, do **not** use your NovolinPen.

DO NOT try to repair a NovolinPen that is not working properly.

(See Warranty section for further information.)

Storage

Guidelines for storing the NovolinPen and PenFill cartridges:

- Store the NovolinPen at room temperature. **Do not store** the NovolinPen in areas where there may be extreme temperatures or moisture, such as in your car.
- Store the NovolinPen **without** the needle attached and **with** the device cap in position.
- The insulin cartridge you are currently using in the NovolinPen can be stored **in the device** at room temperature for the following periods of time:
  - *Novolin R:* 30 days
  - *Novolin 70/30:* 7 days
  - *Novolin N:* 7 days

Such unrefrigerated cartridges must be used within these time periods or discarded.

Any cartridge not currently in use must be stored in a cold place, preferably a refrigerator, but not in the freezer compartment. **Do not let cartridges freeze.**

For more information on storing PenFill cartridges, see the package insert that comes in the PenFill cartridge box.

Maintenance

Guidelines for maintaining the NovolinPen:

Be sure to:

1. Clean it by wiping it with a soft cloth moistened with alcohol.
2. Protect it from dust, dirt, and moisture when not in its case.

Make certain you:

1. **DO NOT** soak it in alcohol, wash it in soap and water, or lubricate it, since this may cause damage.
2. **DO NOT** expose it to excessive pressure or blows.
3. **DO NOT** drop it.

Important Notes

The following is a review of some important information about the use and care of your NovolinPen:

Before each injection, be certain:

1. The NovolinPen contains the correct insulin cartridge, if you use more than one type of insulin.
2. The PenFill cartridge contains at least 12 units, if you use Novolin 70/30 or Novolin N insulin.
3. To always do the air shot with the needle pointing upward.

Be sure to:

1. Keep the locking ring in the unlocked position until you are ready to do an air shot or give an injection.
2. Twist the locking ring into the locked position after dialing the dose. This locks in the dose. No insulin will be injected if the locking ring is in the unlocked position.
3. Reset the dial-a-dose selector to zero after each air shot or injection and before dialing a dose. This makes certain that the correct amount of insulin will be delivered.

4 Remove the PenNeedle from the NovolinPen immediately after each injection.

5 Select your dose only by using the number in the dose indicator window.

6 Perform the function check if you think your NovolinPen is not working properly.

7 Keep out of the reach of children.

Make certain you:

1 **DO NOT** use the NovolinPen without the assistance of a sighted individual trained to use it, if you are blind or visually impaired. NOVOLINPEN IS NOT RECOMMENDED FOR BLIND OR VISUALLY IMPAIRED PATIENTS.

2 **DO NOT** place a needle on the NovolinPen until you are ready to do an air shot and give an injection or perform a function check.

3 **DO NOT** turn the dial-a-dose selector when the locking ring is in the locked position.

4 **DO NOT** twist the locking ring into the locked position until you are ready to do an air shot or give an injection.

5 **DO NOT** use the clicking sound to set your insulin dose.

6 **DO NOT** try to refill a PenFill cartridge.

7 **DO NOT** store the NovolinPen in areas where temperatures may get too hot or cold, such as in a car.

8 **DO NOT** use the same PenFill cartridge for more than one person, even though you attach a new PenNeedle for each injection. This will prevent the spread of disease. Each PenFill cartridge is for single-person use only.

9 **DO NOT** place a PenNeedle on your NovolinPen until you are ready to give an injection; remove it immediately after each injection. If the needle is not removed, some liquid may leak out of the PenFill cartridge. This causes a change in the strength of Novolin 70/30 and Novolin N insulin.

Blood glucose levels should be tested frequently to monitor your insulin regimen.

Any change in brand or type of insulin should be made cautiously and only under medical supervision.

What to Do If...

No droplet appears when you do the air shot.

- The locking ring may still be in the unlocked position. This prevents the pushbutton from going all the way down. (You may feel as if it is moving, but it will spring back. You will not be able to press it all the way down so that it is flat against the top of the dial-a-dose selector.)

  Twist the locking ring 1/4 turn until it is in the locked position and the dots line up.

- The dose may still be set at zero.
  1. *Turn the locking ring to the unlocked position.*
  2. *Dial 2 units.*
  3. *Twist the locking ring 1/4 turn until it is in the locked position and the dots line up.*

- The needle may not be completely attached.
  1. *Put the plastic outer cap back on the needle.*
  2. *Turn the plastic outer cap in a clockwise direction to tighten the needle.*

- The plunger rod may not be fully extended.

  If the plunger rod is not touching the rear rubber stopper, no insulin is forced through the needle when you press the pushbutton.
  1. *Put the plastic outer cap back on the needle to protect it.*
  2. *Turn the locking ring to the unlocked position.*
  3. *Unscrew the clear cartridge casing.*
  4. *Shake down the plunger rod and gently pull it so that it is fully extended (p. 7).*
  5. *Insert the plunger rod into the PenFill cartridge so it rests on the rear rubber stopper* (p. 8).
  6. *Repeat steps 1 through 7* (pp. 12 - 14).

The pushbutton does not rise when you dial the dose.

- When you dial a dose, the pushbutton should rise. The distance it moves away from the top of the dial-a-dose selector determines how much insulin will be delivered.
  Make sure the locking ring is in the unlocked position when you dial the dose.

The device cap is stuck on the clear cartridge casing.

- If you put the device cap on improperly, it may get stuck on the clear cartridge casing.
  Pull the device cap firmly and straight up to remove it.
- If you turn the device cap when you try to remove it, you may unscrew the clear cartridge casing along with it.
  Screw the device cap and the clear cartridge casing back onto the barrel. Then pull straight up on the device cap to remove it.

Warranty

Should your NovolinPen be defective in materials and workmanship at the time it is purchased by a user or within one (1) year of purchase, Novo Nordisk Pharmaceuticals Inc. will replace it at no charge, if the user sends the defective unit, postage prepaid, along with a sales receipt or other proof of purchase to:

Novo Nordisk Pharmaceuticals Inc.
100 Overlook Center
Suite 200
Princeton, NJ 08540-7810

No other warranty is made with respect to NovolinPen.

This warranty will be invalid and Novo Nordisk A/S, Novo Nordisk Pharmaceuticals Inc., Bristol-Myers Squibb Co., Nipro Medical Industries Ltd., and Bang & Olufsen A/S cannot be held responsible in the case of defects or damages arising from:

- The use of the NovolinPen with products other than Novolin PenFill cartridges, PenNeedle single-use disposable needles, or other products specifically recommended by Novo Nordisk.
- The use of the NovolinPen not in accordance with the instructions in this booklet.
- Physical damage to the NovolinPen caused by neglect, misuse, unauthorized repair, accident, or other breakage.

NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES

BUSINESS REPLY MAIL

First Class Mail Permit No 248 Princeton, NJ

POSTAGE WILL BE PAID BY ADDRESSEE:

NovolinPen® Warranty Reply
Novo Nordisk Pharmaceuticals Inc.
100 Overlook Ctr. Suite 200
Princeton, NJ 08540-9827

NovolinPen® Warranty Card

Please indicate the NovolinPen® Serial and Control numbers located on the end of the carton for full NovolinPen® Warranty protection.
Serial: _____ Control: _____

So we may serve you fully, please fill out all of the following information:

Name _____ Age _____ years

Sex _____ M _____ F

Street _____

City _____ State _____

Zip Code _____ Telephone (___) _____

Occupation _____

How long have you had diabetes? _____ years _____ months

How long have you been taking insulin? _____ years _____ months

Have you used Novolin® before? _____ yes _____ no

How did you first hear about NovolinPen®? _____ physician; _____ pharmacist; _____ diabetes educator; _____ diabetes magazine; _____ other (specify) _____

How many times a day do you use NovolinPen®? _____

How many units of insulin do you use daily? _____ units

For assistance or further information, write to:

Novo Nordisk Pharmaceuticals Inc.
Professional Services
100 Overlook Center
Suite 200
Princeton, NJ 08540-7810

Or call: (800) 727-6500

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